

An integrated sustainable medical supply chain network during COVID-19

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ABSTRACT

Nowadays, in the pharmaceutical industry, a growing concern with sustainability has become a strict consideration during the COVID-19 pandemic. There is a lack of good mathematical models in the field. In this research, a production–distribution–inventory–allocation–location problem in the sustainable medical supply chain network is designed to fill this gap. Also, the distribution of medicines related to COVID-19 patients and the periods of production and delivery of medicine according to the perishability of some medicines are considered. In the model, a multi-objective, multi-level, multi-product, and multi-period problem for a sustainable medical supply chain network is designed. Three hybrid meta-heuristic algorithms, namely, ant colony optimization, fish swarm algorithm, and firefly algorithm are suggested, hybridized with variable neighborhood search to solve the sustainable medical supply chain network model. Response surface method is used to tune the parameters since meta-heuristic algorithms are sensitive to input parameters. Six assessment metrics were used to assess the quality of the obtained Pareto frontier by the meta-heuristic algorithms on the considered problems. A real case study is used and empirical results indicate the superiority of the hybrid fish swarm algorithm with variable neighborhood search.

1. Introduction

COVID-19 is an acute respiratory disease caused by acute respiratory syndrome (Shirazi et al., 2020). The mortality rate of this disease is estimated between 1% and 5%, which varies according to the physiological characteristics of the patient (Chen et al., 2020a; Vega, 2020). The disease is transmissible based on the microbial droplets of the infected person and has a higher incidence rate than other infectious diseases (Chen et al., 2020b; Liu et al., 2020a,b). However, a definitive cure for the disease has not yet been discovered, but tests suggest that medicines such as RamedSivir and Favipiravir can reduce the side effects of COVID-19 disease (Lauer et al., 2020). Hence, the number of infected people, the number of deaths, and the number of the total recovered due to this disease in different countries are reported in Table 1.

According to the current critical situation, it seems necessary to design an appropriate medicine supply chain network that can provide appropriate medicines to COVID-19 patients in an organized manner (Kairon and Bhattacharyya, 2020). Therefore, inventory control and management of medicine distribution in such conditions due to the perishability of medicines can reduce human casualties and increase the health of patients (Nilashi et al., 2020). In addition, uncertainty in

the supply chain network of medicine distribution is an integral part. The demand in hospitals for various medicines is scattered and should always be seen with uncertainty (Mardani et al., 2020). For this reason, the sensitivity of work in completing this supply chain increases. In this regard, the location of medicine distribution centers can also accelerate the service to patients and reduce supply chain costs. In addition to the mentioned above, paying attention to a sustainable supply chain can lead to more flexibility and closer the problem to the real world.

The raising concerns to meet social and environmental necessities during the COVID-19 pandemic are forcing hospitals/pharmacies to consider the impacts of sustainable supply chain network design on the society and environment (Majumdar et al., 2020). A significant concept in sustainability is the social responsibility of staff (nurses and doctors) in hospitals, pharmacies, and laboratories. Social responsibility is the effect of hospitals, pharmacies, and laboratory activities on diverse groups which includes workplace safety, environmental conservation, right conditions for staff, job creation, and economic regional development, etc.

In this paper, a new multi-objective, multi-product, and multi-echelon mathematical formulation called Sustainable Medical Supply Chain Network (SMSCN) during the COVID-19 pandemic is developed.

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Table 1

The number of the total death, the infected case, the number of the total recovered on 01/23/2021 (World Health Organization, 2020).

Country	Total confirmed cases	Total recovered	Total deaths
China	88911	82562	4635
United States of America	25390042	15222719	424177
Iran	1360852	1151676	57225
Brazil	8755133	7594771	215299
Russia	3677352	3081536	68412
India	10640544	10300063	153221
Spain	2603472	1987654	55441
Italy	2441854	1855127	84674
UK	3583907	1600622	95981
Germany	2125261	1780200	52020

Also, this network is provided in order to the location of distribution centers, inventory management, and the planning of allocation centers in the COVID-19 pandemic condition. A new mixed-integer linear programming model according to the SMSCN problem during the COVID-19 pandemic is formulated. Additionally, the three pillars of sustainability are considered including economic, environmental, and social effects. Moreover, another important contribution in this paper is to minimize the total costs (transportation, establishing, operating, inventory, and production costs), manage the unsatisfied demand for medicines, environmental effects (the released CO₂ emission through established distribution center during medicine transportation) along with maximization of social factors and job creation in established distribution centers during the COVID-19 pandemic. Due to the uncertainty of medicine demand during the COVID-19 pandemic, the simulation approach has been used to calculate the demand distribution function of the required medicines for the first time in this paper. Accordingly, another important contribution of this study, after estimating the medicine demand distribution function, this parameter enters the mathematical model, which is called the simulation–optimization approach. To solve the SMSCN problem (which is NP-hard), three swarm intelligence based meta-heuristic algorithms: Ant Colony Optimization (ACO), Fish Swarm Algorithm (FSA), and Firefly Algorithm (FA) are hybridized with variable neighborhood search (VNS), namely, HACO-VNS, HFSA-VNS, and HFA-VNC are used. To tuning of parameters of the proposed algorithms is achieved using the response surface method. To validate the SMSCN model, six assessment metrics are used. They are Hyper Volume (HV), Number of Pareto Solutions (NPS), Mean Ideal Distance (MID), Maximum Spread (MS), Inverted Generational Distance (IGD), and Spread of Non-Dominance Solution (SNS). A real case study is provided and a set of sensitivity analyses on important parameters are illustrated.

The rest of this paper is organized as follows. In Section 2, the literature review, and relevant research in the medicine SMSCN problem have been discussed. Section 3 describes the problem definition of the SMSCN during the COVID-19 pandemic. The simulation model for the medicine SMSCN problem is explained completely in Section 4. Section 5 defines the mathematical model for the SMSCN problem. Additionally, the multi-objective solution technique is presented in Section 6. Section 7 illustrates the proposed solution methodology and encoding scheme and initialization. Computational experiments, assessment metrics, parameters setting (response surface method), comparison of the proposed algorithms (Pareto optimal analysis), simulation results, case study to validate the SMSCN model, sensitivity analysis, What-If analysis, discussion, and managerial insights are provided in Section 8. Eventually, Section 9 contains conclusions and future works.

2. Literature review

In this research, we developed a novel solution methodology to cope with the sustainable medical supply chain network (SMSCN) network

design. The literature is focused on SMSCN models during the COVID-19 pandemic and on analyzing their solutions, especially those utilizing meta-heuristic algorithms.

Weraikat et al. (2016) extended the reverse medicine supply chain network by considering customer incentives. In their research, a cooperation mechanism has been defined for coordination between medicine manufacturers and third-party logistics. The medicines are sent directly to the customers by the distributors and in the reverse path, the perishable medicines are sent to the burial center by the third-party. A hybrid simulation–optimization approach to design the medicine distribution network and medical equipment is suggested by Martins et al. (2017). A mixed-integer linear programming model was used for strategic stage decisions and a discrete event simulation model for operational stage decisions is considered. To minimize transportation costs, inventory holding, and operating costs are the most important objective functions of their proposed model. The results show that with increasing demand, system costs also increase sharply. Then, a simulation–optimization model for strategic and operational decisions in the chemical-pharmaceutical industry is presented by Marques et al. (2017). For supply chain network simulation, Monte Carlo two-step simulation based on Bernoulli and Normal distributions were used. The considered planning phases include discovery, preclinical, approval, manufacturing, and distribution. Determining the amount of required raw materials, batch size, delivering medicine, and allocation manufacturers to medical centers were the most important decisions of their model. Zahiri et al. (2017) designed a sustainable medicine supply chain network. The main goal of their research is the location of medicine production and distribution centers along with inventory control of medicines in the centers. In their model, the possibilistic–stochastic programming approach has been used to deal with uncertain parameters. The Pareto-based lower bound method approach has been used to solve the case study. Sánchez et al. (2017) designed an optimization approach for modular neural network and proposed a firefly algorithm that the results of the firefly algorithm compared with hierarchical genetic algorithm. Zahiri et al. (2018) provided a hierarchical mathematical model for designing a medicine supply chain network. Then, considering medicine perishable, stability, and the number of discounts on medicine purchases has been considered in their contributions. The main purpose of their paper is to minimize total costs while minimizing unsatisfied demand. To deal with the uncertainty parameter, the robust possibilistic approach has been used. Nasrollahi and Razmi (2019) designed an integrated supply chain network to maximize expected coverage. A four-level model is provided includes manufacturer, distributor, hospital, and patients. The main aim of their model is to minimize supply chain costs while maximizing chain reliability. To solve the case study in Fars/Iran, two approaches of Particle Swarm Optimization and Non-Dominated Sorting Genetic Algorithm II have been used. Fathollahi-Fard et al. (2020) presented a fuzzy multi-objective and multi-period mathematical model for routing and scheduling the home healthcare problem. The considered levels include pharmacies, laboratories, and patients. Also, customer satisfaction under uncertainty is considered one of the contributions of their research. To solve the proposed model, the social engineering optimizer algorithm and the modified SEO approach adaptive memory strategy have been used. The results indicate the proper performance of the proposed solution approaches. Akbarpour et al. (2020) formulated a mathematical model for the distribution of perishable medicines in post-disaster conditions. Locating mobile pharmacies and suppliers, determining the amount of the inventory of hospitals and pharmacies, and determining the amount of unmet demand are among the decisions made in their research. In their study, the demand for relief medicines was considered as a potential one and the cooperative coverage mechanism was used to distribute the medicines. The min-max robust approach has been used to deal with the natural uncertainty of the problem. Goodarzian et al. (2020b) developed a multi-objective mathematical model for the production, purchase, and distribution of

essential medicines. Routing medicine distribution vehicles, allocation distribution centers to pharmacies, and inventory control of distribution centers are considered their contributions. Purchasing, ordering, and delivery costs are considered as uncertain parameters. To cope with uncertain parameters, fuzzy-robust programming has been used. To solve their proposed model, multi-objective social engineering optimization, simulated annealing, Keshlre algorithm, and firefly algorithm meta-heuristic approaches have been utilized. Franco and Alfonso-Lizarazo (2020) designed a stochastic simulation-optimization model for operational and strategic decisions in the medicine supply chain. For this purpose, two mathematical models have been considered with the levels of hospital and pharmacy. In the first model, the expiration date and level of service were considered, while their aims were inventory control decisions and select a supplier. Then, the case scenarios are generated with the simulation model. The second model is a bi-objective model that aims to minimize the number of delivered perishable medicines. Tat et al. (2020) developed a mathematical model for minimizing costs in the medicine supply chain network. The proposed network has bi-level and includes pharma-suppliers and pharmacies. In their study, some of the perishable medicines are bought and the rest is buried. The decentralized decision-making approach has been used for mathematical modeling. The results indicate the proper performance of the proposed model.

It should be mentioned here that there are many papers with various features on SMSCN. To control more examined studies, a set of meta-heuristic algorithms works will be examined. On the other hand, since utilizing meta-heuristic algorithms is the most suitable method in tackling such NP-hard problems, there are several previous papers in this field. Instances contain Devika et al. (2014), Vahdani et al. (2017), Sabouhi et al. (2018), Fakhrazad et al. (2018), Mani and Gunasekaran (2018), Fakhrazad et al. (2019), Roshan et al. (2019), Ghasemi et al. (2019), Goodarzian and Hosseini-Nasab (2019), Govindan et al. (2019), Viegas et al. (2019), Halim et al. (2019), Zandkarimkhani et al. (2020), Ghasemi and Khalili-Damghani (2020), Liu et al. (2020a,b), Goodarzian et al. (2020a), Ghasemi et al. (2020), Ang et al. (2020), Goodarzian et al. (2020b), Goodarzian et al. (2021), and Fathollahi-Fard et al. (2020).

Castillo and Melin (2020) presented a hybrid intelligent method for forecasting COVID-19-time series combining fuzzy logic and fractal theory that was the main contribution of their paper. Fuzzy logic employed to show the uncertainty in the process of making a forecast and the fractal dimension utilized to measure the complexity of the dynamics in the time series of the countries in the world. They presented a hybrid method including a fuzzy model by a set of fuzzy rules that utilize as input values for the nonlinear and linear fractal dimensions of the time series as well as indicated results the forecast for the countries according to the COVID-19-time series for confirmed cases and deaths. Sun and Wang (2020) developed the simulation utilizing this trained model to characterize the effect of an imported 'escaper'. Then, they indicated an imported 'escaper' was responsible for the newly confirmed COVID-19 infections from April 9 to 19 in Heilongjiang province. Stochastic simulations further indicated that importantly increased local contacts between imported 'escaper', its epidemiologically associated cases, and susceptible populations greatly contributed to the local outbreak of COVID-19. Likewise, they further received that the reported number of asymptomatic patients was markedly lower than model predictions implying a large asymptomatic pool that was not identified. Golan et al. (2020) stated a literature review applications and trends of resilience analytics in supply chain modeling in the context of the COVID-19 pandemic. Kumar et al. (2020a,b) analyzed the social and economic aspects of COVID-19 on specific dimensions of the global economy. Therefore, insights about the effects of the pandemic on different fields such as the medical industry, information technology, agriculture, manufacturing, finance, and many others are presented. These insights may support strategic decision making and policy framing activities for the high-level management in the private

and government sectors. Varela-Santos and Melin (2020) provided a new method for classifying coronavirus COVID-19 according to its manifestation on chest X-rays utilizing texture characteristics and neural networks. In addition, a series of tests utilizing supervised learning models to perform classification on datasets including medical images of several other relevant diseases affecting the lungs and medical images from COVID-19 patients. Their aim was to set a baseline for the future development of a system capable of automatically detecting the COVID-19 disease according to its manifestation on chest X-rays and computerized tomography images of the lungs. There are several papers that examined the concepts of sustainability during the COVID-19 pandemic including Rume and Islam (2020), Silva et al. (2020), Vanapalli et al. (2020), Kumar et al. (2020a,b), Severo et al. (2020), Mori et al. (2020), Taqi et al. (2020), Shirvani Dastgerdi et al. (2021).

Eventually, the research contributions and novelties of this paper are stated as follows:

- In terms of mathematical modeling, the lack of a proper multi-level, multi-objective, multi-product, multi-period problem for designing an SMSCN model during the COVID-19 pandemic is specified. In this regard, in this paper, a new mathematical modeling based on the location-distribution-allocation-inventory control-production problem in an SMSCN model during the COVID-19 pandemic is developed. Then, a new mixed-integer linear programming model considering distribution medicines related to COVID-19 patients and the periods of production and delivery of medicine according to the possibility of perishable of some medicines is formulated and designed.
- Next, a new integrated simulation-based optimization technique for the SMSCN problem is developed. Along the way, there is the uncertainty of medicine demand during the COVID-19 pandemic that the simulation method is used to compute the demand distribution function of the needed medicines for the first time in this paper.
- After that, to solve the model and find the Pareto solutions, three new hybrid meta-heuristic algorithms are developed by considering the neighborhood structure (NS) of the VNS in the search process in order to optimize the problems. Moreover, three methods called HACO-VNS, HFSA-VNS, and HFA-VNS algorithms are extended that are used to solve the proposed model during the COVID-19 pandemic.
- Finally, a simulation approach, a response surface method, six assessment metrics such as HV, NPS, MID, MS, IGD, and SNS metrics, a real case study, and some sensitivity analysis are illustrated to validate the suggested model.

Therefore, Fig. 1 indicates the research framework for describing the procedure of optimization process.

3. Problem description

In this research, a new four-echelon multi-product multi-period mixed-integer linear programming (MILP) model for the problems of location, production, distribution, allocation, and inventory control of medicines related to COVID-19 treatment in the sustainable supply chain network (SMSCN) is developed. Therefore, first, the medicines are produced by laboratories and delivered to permanent centers. Permanent centers at this stage perform a series of operations that make the medicine usable for patients. Then, the medicines are sent to distribution centers (DCs). It should be noted that in case of a shortage of medicine at this stage, it is possible to transfer the medicine between DCs. Eventually; the medicines will be distributed among hospitals by DCs. The location of DCs, determining the number of medicines flowing between supply chain levels, the amount of stored inventory in each echelon of the chain, and the shortages and surpluses of stored medicines in each hospital are among the decisions that are considered in this study. DCs are also considered at different capacity

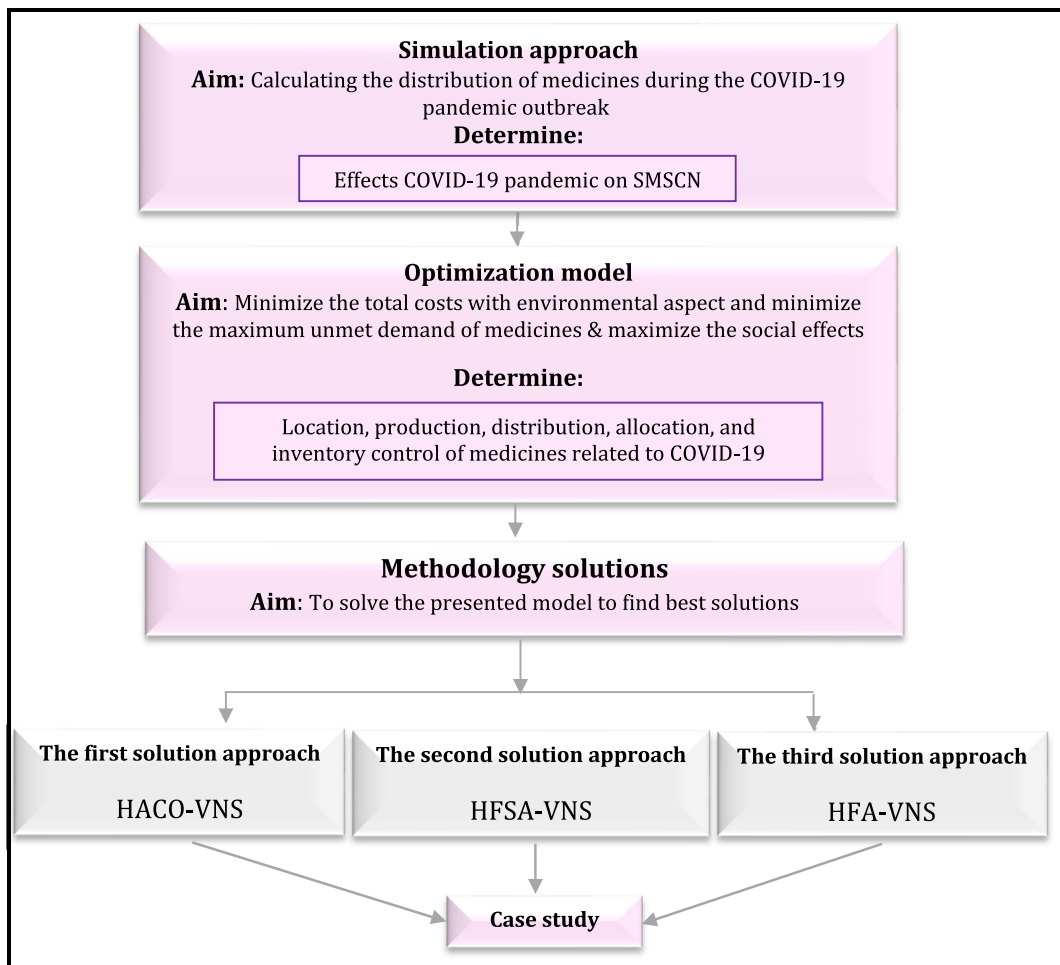


Fig. 1. Research framework.

levels including small, medium, and large. In hospitals, in case of shortage, it is possible to substitute similar medicines, which makes the problem more flexible and closer to the real world. Hence, considering the periods of production and delivery of medicine according to the possibility of perishable of some medicines is one of the significant contributions in this study. This will prevent the perishable of the medicines as much as possible. Another important contribution that has been considered in this paper is the sustainability in the supply chain network (SCN) problem during distributing medicines related to COVID-19 patients. Therefore, first of all, the costs of established DCs, inventory holding, transportation costs, and the costs of shortages and surpluses are tried to minimize. Additionally, the generated environmental impacts through established DCs and the transportation of COVID-19 medicines are sought to decrease. Finally, social factors and job creation in established DCs are among the other contributions that have been considered in this research. The framework of the developed SCN related COVID-19 is shown in Fig. 2.

4. Simulation model for SMSCN problem

In this section, the structure of the dynamic development system of COVID-19 in the community is shown in Fig. 3. The three considered loops include infection (R1), social distancing (B), and screening capacity (R2). Then, considered stocks in this study include susceptible, early infected, late infected, recovered, and dead. As it is clear that in R1, suspects are exposed to COVID-19 at an infectious rate. The following three conditions occur for the late infected. (i) The first case is the death of patients, (ii) The second case is the recovery of patients, and (iii)

The third case is the diagnosis of COVID-19 disease and quarantine of patients. Patients may also die or pass the disease on to others at a contact rate. The proposed structure will estimate the number of people with COVID-19 based on defined variables and stocks.

Therefore, the simulation structure of estimating the amount of required medicine for COVID-19 patients is depicted in Fig. 4. The simulation of the proposed structure is performed by Enterprise Dynamic (ED) software. ED software is defined by atoms and 4Dscript codes can simulate a variety of real-world problems. Many successful applications of simulation have been reported by this software (Ghasemi and Khalili-Damghani, 2020). To simulation model of the proposed structure consists of 17 atoms, 15 servers, a source, and 1 sink. The source atom is responsible for entering the input into the system and the sink is responsible for completing the input stream. Also, server atoms are used to examine interactions between agents, which contain 4Dscript codes. The “confirmed infected” server is responsible for estimating the number of people with COVID-19 and the “medicine” server is responsible for estimating the amount of needed medicine for each patient. The proposed model is implemented for 3,000,000 h and the warm-up period is equal to 300,000 h. The type of used simulation was also a separate run.

Furthermore, the structure of the “medicine” server is demonstrated in Fig. 5. As it is known, the value of cycle time is considered as a negative exponential with an average of 10 s. Also, according to the entered 4Dscript in this server, the amount of required medicine for each infected person is considered to be 0.3 kg. It should be noted that the considered performance measurement (PFM) is AvgContent (cs), which estimates the average input per atom and leads to the prediction of the amount of required medicine for patients with COVID-19.

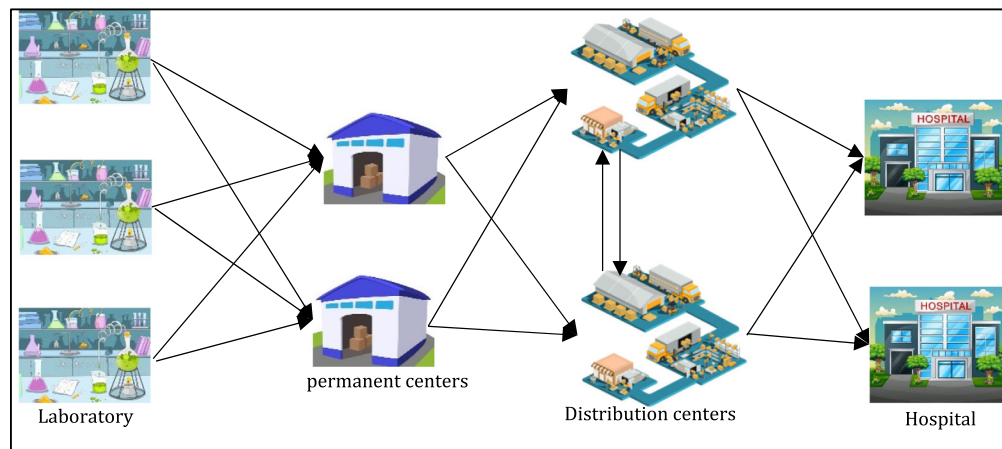


Fig. 2. The framework of the developed SMSN related COVID-19.

Hence, the notations utilized the formulation of our developed model is defined in the following subsections.

5. Mathematical model for SMSN problem

5.1. Sets

h	Index of hospital $h \in H$
g	Index of permanent center $g \in G$
i	Index of the medicine production laboratory $i \in I$
m, m'	Index of the types of medicine $m, m' \in M$
l	Index of the capacity level of the distribution center
w	Index of the location of the established distribution center $w \in W$
e	Index of the period of shipping medicine $e, \dots, E \in T$
r	Index of the period of medicine production $r, \dots, R \in T$
t	Index of the periods $t \in T$

5.2. Parameters

em_{wl}	The released CO ₂ cost through established DC w with the capacity level l
cr_m	The released CO ₂ cost through a unit medicine shipping m in the one KM
ma'_{ml}	The mass of one unit of type m medicine stored in DC with capacity level l
ma_{mw}	The mass capacity of DC w to store type m medicine
vol_{mw}	The volumetric capacity of DC w for medicine m
vol'_{ml}	The volume of one unit of medicine m in DC with capacity level l
nf_w^l	The number of created fixed jobs in the establishment DC w with capacity level l
nv_w^l	The number of created variable jobs in the establishment DC w with capacity level l
we	Importance of job opportunity criteria
we'	Importance of economic development criteria
rw_w	Unemployment rate of established DC w
Bd_g	Available budget to permanent centers g
ew_w^l	The economic value of the location of the establishment DC w with capacity level l
rd_w	The level of regional development in an established DC w
ps_{mh}	Penalty of medicine m shortage in hospital h
psu_{mh}	Penalty of medicine m surplus in hospital h
s_{mh}	Upper bound of the penalty of medicine m shortage in hospital h

cp_{gm}	The storage capacity of medicine m in permanent center g
$cw'_{ww'm}$	Transportation cost of medicine m between DCs w and w'
cw_{whm}	Transportation cost of medicine m between DC w hospital h
ct_{gwm}	Transportation cost of medicine m between permanent center g and DC w
cs_{wl}	The establishing cost of DC w with capacity level l
co_{wl}	The operating cost of DC w with capacity level l
f_{gm}	Inventory cost of medicine m in permanent center g
pc_{mit}	Production cost of medicine m in the medicine production laboratory i at the period t
pr_{mh}	The importance medicine m in hospital h
d_{hmt}	The demand of medicine m in hospital h at the period t
j_m	The holding time of medicine m
$sm_{mm'}$	Medicine substitution matrix m instead of m' . 1 if it can be replaced, otherwise 0

5.3. Decision variables

I'_{wmtr}	The amount of inventory medicine m in DC w at the period t which are produced at the period r and are shipped at the period e .
I_{gmtr}	The amount of inventory medicine m in permanent center g at the period t which are produced at the period r
A_{mit}	The amount of medicine m produced in the medicine production laboratory i at the period t
$H_{ww'mt}$	Medicine flow m between the DCs w and w' at the period t
y'_{mht}	Surplus of type m medicine in hospital h at the period t
y''_{mht}	The amount of medicine shortage m in hospital h at the period t
l_{gt}^m	The amount of medicine inventory m in permanent center g at the period t
x_{igt}	Medicine flow m between laboratory i and permanent center g at the period t
x^1_{mhw}	Medicine flow m between DC w and hospital h at the period t
x^2_{mgwt}	Medicine flow m between permanent center g and DC w at the period t
f_{whmret}	Medicine flow m between DC w and hospital h at the period t , which are produced at the period r and are shipped at the period e

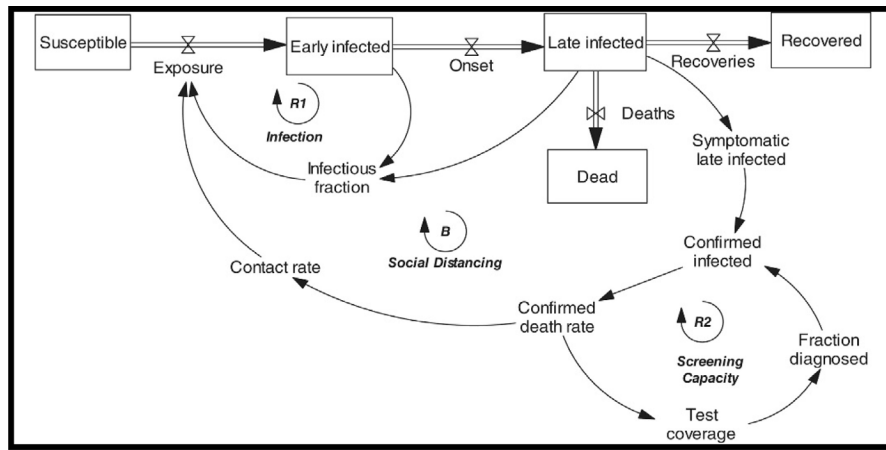


Fig. 3. The structure of the developed dynamic system COVID-19.

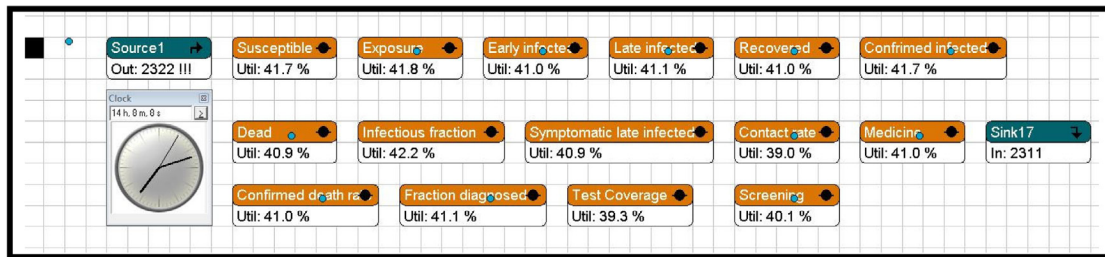


Fig. 4. The proposed simulation structure in ED software.

- Q_{gwmrt} Medicine flow m between permanent center g and DC w at the period t , which are produced at the period r
- $O_{ww'mret}$ Medicine flow m between DCs w and w' at the period t , which are produced at the period r and are shipped at the period e
- y_{wl} 1 if the DC w is established with capacity level l , otherwise 0.
- Z_{git} 1 if permanent center g is allocated to laboratory i at the period t , 0 otherwise
- Z_{wgt} 1 if DC w is allocated to permanent center g at the period t , 0 otherwise
- Z_{hwt} 1 if hospital h is allocated to DC w at the period t , 0 otherwise

5.4. Mathematical model

$$Max f_1 = we(\sum_w \sum_l (nf_w^l + nv_w^l)rw_w y_{wl}) + we'(\sum_w \sum_l ew_w^l(1 - rd_w)y_{wl}) \tag{1}$$

$$Min f_2 = \sum_l \sum_w csw_{wl}y_{wl} + \sum_{gmt} \sum_{r=1} f_{gm}I_{gmr} + \sum_{wmt} \sum_{e=r} \sum_{l=1} c_{ow_{wl}}I'_{wmtre} + \sum_{gumt} c_{gm}^l x_{mgwt}^2 + \sum_{whmm't} c_{w_{whm}} sm_{mm't} x_{mwht}^1 + \sum_{w'w'hmt} c_{w'_{w'w'm}} H_{w'w'mt} + \sum_h \sum_m y'_{mh} pr_{mh} ps_{mh} + \sum_h \sum_m y'_{mh} ps_{mh} + \sum_{whmm't} c_{r_m} sm_{mm't} x_{mwht}^1 + \sum_{w'w'hmt} c_{r_m} H_{w'w'mt} + \sum_{gumt} c_{r_m} x_{mgwt}^2 + \sum_l \sum_w em_{wl} y_{wl} + \sum_m \sum_i \sum_t pc_{mit} A_{mit} \tag{2}$$

$$Min f_3 = Max_{hmt} pr_{mh} [d_{hmt} - \sum_{wm't} sm_{mm't} x_{mwht}^1] \tag{3}$$

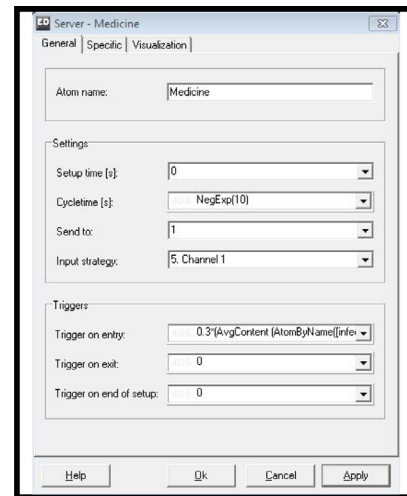


Fig. 5. Server atom settings.

The first objective function (1) investigates to maximize social factors, job creation, and economic regional development. The second objective function (2) minimizes the costs of establishing DCs, inventory holding, transportation costs, production cost in the medicine production laboratory, shortage, and surplus costs. Also, this function decreases the cost of released carbon dioxide from the establishment of DC and the transportation of medicine. The third objective function (3) decreases that the maximum unmet demand for medicines.

$$y'_{mht} \geq \sum_w x_{mwht}^1 - d_{hmt} \quad \forall h, m, t \tag{4}$$

$$y'_{mht} \leq d_{hmt} - \sum_w x_{mwht}^1 \quad \forall h, m, t \tag{5}$$

$$I_{gmt} = I_{gmt-1r} - \sum_w Q_{gwmrt} \quad \forall g, r, m, t - r \geq j_m \quad (6)$$

$$I_{gmt} = \sum_i x_{igmt} - \sum_w Q_{gwmrt} \quad \forall g, m, t, r = t \quad (7)$$

$$\sum_{r=1}^t I_{gmt} = \sum_i x_{igmt} - \sum_w x_{mgwt}^2 \quad \forall g, m, t = 1 \leq j_m \quad (8)$$

$$\sum_{r=1}^t I_{gmt} = \sum_{r=1}^{t-1} I_{gmt-1r} + \sum_i x_{igmt} - \sum_w x_{mgwt}^2 \quad \forall g, m \quad 1 \leq t \leq j_m \quad (9)$$

$$\sum_{r=t+1-j_m}^t I_{gmt} = \sum_{r=t+1-j_m}^t I_{gmt-1r} + \sum_i x_{igmt} - \sum_w x_{mgwt}^2 \quad \forall g, m, t \geq j_m \quad (10)$$

$$x_{mgwt}^2 = \sum_{r=1}^t Q_{gwmrt} \quad \forall g, m, w, t \leq j_m \quad (11)$$

$$x_{mgwt}^2 = \sum_{r=t+1-j_m}^t Q_{gwmrt} \quad \forall g, m, w, t \geq j_m \quad (12)$$

$$\sum_i x_{igmt} \leq cp_{gm} \quad \forall g, m, t \quad (13)$$

$$M_{ww'mt} = \sum_{e=r}^{r+j_m-1} \sum_{r=1}^t O_{ww'mret} \quad \forall w, w', m, t < j_m \quad (14)$$

$$M_{ww'mt} = \sum_{e=r}^{r+j_m-1} \sum_{r=1}^t O_{ww'mret} \quad \forall w, w', m, t \geq j_m \quad (15)$$

$$I'_{wmtre} = I'_{wmt-1re} - \sum_h f_{whmret} + \sum_{w'} O_{ww'mret} \quad \forall w, m, r, e, t, e \neq t \quad (16)$$

$$I'_{wmtre} = \sum_g E_{gwmrt} - \sum_h f_{whmret} + \sum_{w'} O_{ww'mret} - \sum_{w'} O_{ww'mret} \quad \forall w, m, r, e, t, e = t \quad (17)$$

$$\sum_{e=1}^t \sum_{r=1}^t I'_{wmtre} = \sum_g x_{mgwt}^3 - \sum_h x_{mwht}^1 + \sum_{w'} H_{ww'mt} - \sum_{w'} H_{w'wmt} \quad \forall w, m, t = 1 \leq j_m \quad (18)$$

$$\sum_{e=1}^t \sum_{r=1}^t I'_{wmtre} = \sum_{e=r}^{t-1} \sum_{r=1}^{t-1} I'_{wmt-1re} - \sum_h x_{mgwt}^2 - \sum_h x_{mwht}^1 + \sum_{w'} H_{w'wmt} - \sum_{w'} H_{ww'mt} \quad \forall w, m, 1 \leq t \leq j_m \quad (19)$$

$$\sum_{e=r}^{r+j_m-1} \sum_{r=t-j_m+1}^t I'_{wmtre} = \sum_{e=r}^{t-1} \sum_{r=t-j_m+1}^{t-1} I'_{wmt-1re} + \sum_g x_{mgwt}^2 - \sum_h x_{mwht}^1 + \sum_{w'} H_{w'wmt} - \sum_{w'} H_{ww'mt} \quad \forall w, m, t \geq j_m \quad (20)$$

$$x_{mwht}^1 = \sum_{e=r}^t \sum_{r=1}^t f_{whmret} \quad \forall w, h, m, t < j_m \quad (21)$$

$$x_{mwht}^1 = \sum_{e=r}^t \sum_{r=t-j_m+1}^t f_{whmret} \quad \forall w, h, m, t \geq j_m \quad (22)$$

$$\sum_h x_{mwht}^1 \leq \sum_g x_{mgwt}^2 \quad \forall w, m, t \quad (23)$$

$$\sum_w x_{mwht}^1 y_{wh} - d_{hmt} = y'_{mht} - y''_{mht} \quad \forall t, h', m, h, h \neq h' \quad (24)$$

$$\sum_{m'} sm_{mn'} x_{mwht}^1 \leq x_{mwht}^1 \quad \forall w, h, m, t \quad (25)$$

$$\sum_{gm} \sum_l x_{mgwt}^2 ma'_{ml} + \sum_{w'm} \sum_l H_{ww'mt} ma'_{ml} \leq \sum_m \sum_l ma_{mw} y_{wl} \quad \forall w, t \quad (26)$$

$$\sum_{gm} \sum_l x_{mgwt}^2 vol'_{ml} + \sum_{w'm} \sum_l H_{ww'mt} vol'_{ml} \leq \sum_m \sum_l vol_{mw} y_{wl} \quad \forall w, t \quad (27)$$

$$\sum_l z_{wl}^1 \leq 1 \quad \forall w \quad (28)$$

$$\sum_w x_{mgwt}^2 \leq l_{gt}^m \quad \forall g, m, t \quad (29)$$

$$x_{mgwt}^2 \leq l_{gt}^m \sum_l y_{wl} \quad \forall g, w, m, t \quad (30)$$

$$\sum_l \sum_w (\sum_i cow_{wl} + cs_{wl}) y_{wl} + \sum_g \sum_w \sum_m (\sum_t x_{mgwt}^2 ct_{gwm}) \leq \sum_g Bd_g \quad (31)$$

$$\sum_i Z_{git} \leq 1 \quad \forall g, t \quad (32)$$

$$\sum_g Z_{wgt} \leq 1 \quad \forall w, t \quad (33)$$

$$\sum_w Z_{hwt} \leq 1 \quad \forall h, t \quad (34)$$

$$A_{mit} = x_{igmt} \quad \forall m, i, g, t \quad (35)$$

$$f_{whmret}, O_{gwmrt}, O_{ww'mret}, I_{gmt}, I'_{wmtre}, l_{gt}^m, H_{ww'mt}, x_{igmt}, x_{mwht}^1, x_{mgwt}^2, y'_{mht}, y''_{mht} \geq 0 \quad \forall g, m, m', e, h, i, l, w, r, t \quad (36)$$

$$y_{wl}, Z_{git}, Z_{wgt}, Z_{hwt} = \{0, 1\}$$

Constraints (4) and (5) show the upper bound of shortage and the lower bound of surplus medicines in each hospital. Constraint (6) indicates the connection between inventory during a period and previous period. Then, the amount of balance of permanent centers' inventory based on the time period of medicine production is shown in constraint (7). This amount is equal to the amount of medicine input from the laboratory to the permanent center (x_{igmt}) minus the amount sent from the permanent center to DC. Constraints (8) and (9) demonstrate that the amount of inventory of permanent centers at a time period should be less than the period of medicine perishable. As it is clear that, the constraint (8) is only for the first period and the constraint (9) is for the first period until the time of perishable. The reason for this is the entered inventory level into permanent centers in previous periods. Also, in constraint (10), the level of inventory of permanent centers is displayed if the period of time is more than the period of medicine perishable. Constraint (11) illustrates the flow of the medicine from the permanent center to DC in a case where the time period is less than the period of medicine perishable. On the other hand, in constraint (12), the flow of the medicine from the permanent center to the DC in a case where the time period is more than the period of medicine perishable is indicated. Additionally, the storage capacity of each medicine in each permanent center is shown in constraint (13). Constraints (14) and (15) reveal the transferred medicine between DCs according to its production period. In constraints (16) and (17), the inventory of medicines in DCs according to the delivery period is determined. As it is known, when $e \neq t$, it shows the inventory of this period is equal to the inventory of previous periods minus the sent inventory to another DC. In this regard, the level of medicine inventory in the amount of DCs' inventory in conditions where the time period is less than the period of medicine perishable is demonstrated in constraints (18) and (19), while constraint (18) is only for the first period and constraint (19) is for period 1 until the time of perishable. Constraint (20) also indicates the level of inventory of DCs if the time period is more than the time period of medicine perishable. Constraints (21) and (22) indicate the sent medicine from DC to the hospital according to its production period. Constraint (23) ensures that the amount of transported medicine from DC to the hospital must be less than the amount of transported medicine from the permanent center to that DC. Therefore, the amount of shortage and surplus of medicine in each hospital is indicated in constraint (24). Constraint (25) demonstrates that the number of substituted medicines should not exceed the total number of transferred medicines from DC to the hospital. Constraints (26) and (27) determine the mass and volume capacity of DCs. Constraint (28) ensures that each DC is established at only one capacity level. Constraint (29) indicates that the amount of sent medicine from the permanent center to DC must be less than the inventory level of that permanent center. Constraint (30) ensures that medicines are

shipped from the permanent center to DC if DC is pre-established. Then, the budget for permanent centers is shown in constraint (31). Constraints (32)–(34) show allocation constraints between network levels. Constraint (35) indicates all production medicines should be sent to permanent centers. Finally, in constraint (36), the sort of decision variables and their range is determined.

6. Multi-objective solution technique

Generally, multi-objective meta-heuristics provide a trade-off among conflicting objective functions that result in a set of optimal non-dominated solutions called Pareto-optimal solutions, while meta-heuristics for single-objective problems upon attaining a single optimal solution are demonstrated. Any objective is able to modify only at the cost of ruining another objective/s according to each Pareto-optimal solution. Therefore, the decision-makers articulated a posterior preference or prior over objectives based on Multi-objective techniques. Hence, scalarization in multi-objective problems for converting to a single-objective problem is a general procedure to solve multi-objective optimization problems. All in all, the following equation changes the problem to the single objective space for maximization of (37) and minimization of (38):

$$\left[\sum_{j=1}^2 \left(\frac{k_j^* - k_j(x)}{x_j^*} \right)^p \right]^{\frac{1}{p}} \tag{37}$$

$$\left[\sum_{j=1}^2 \left(\frac{z_j(y) - z_j^*}{z_j^*} \right)^p \right]^{\frac{1}{p}} \tag{38}$$

where k_j^* and z_j^* are the maximum and minimum value of the j th objective and then the problem with only the j th objective is solved. The largest deviation according to the increasing the p is devoted. Moreover, a challenge of this procedure includes the detection of a proper value for p (a value that fits the attitude of the decision-maker). According to the priority of expressed decision-makers by p , this procedure generates a single Pareto solution. Additionally, the aforementioned procedure with the weighting method utilizing is combined in order to generate a Pareto front while is formulated as follow:

$$\left[\sum_{j=1}^2 m_j \left(\frac{k_j^* - k_j(x)}{x_j^*} \right)^p \right]^{\frac{1}{p}} \tag{39}$$

$$\left[\sum_{j=1}^2 m_j \left(\frac{z_j(y) - z_j^*}{z_j^*} \right)^p \right]^{\frac{1}{p}} \tag{40}$$

where m_j is the weight related to the j th objective that should be satisfied as follows:

$$\sum_{j=1}^2 m_j = 1 \tag{41}$$

Accordingly, the Pareto frontier will be generated based on changing these weights.

7. Presented hybrid meta-heuristic algorithms

To find the best design of SMSCN, few hybrid algorithms are used in this paper. All the meta-heuristics are hybridized with a variable neighborhood search (VNS) as a local search for a fair comparison between the presented algorithms. The presented meta-heuristics include HACO-VNS, HFSA-VNS, and HFA-VNC of a hybrid of Ant Colony Optimization (ACO), Fish Swarm Algorithm (FSA), and Firefly Algorithm (FA) algorithms with VNS algorithm. Original meta-heuristic algorithms are powerful algorithms in local search but at times it may trap into some local optima so that they cannot perform global search well. For this reason, the hybrid meta-heuristic algorithms possess a better capability

to escape from local optimums with faster convergence than the original meta-heuristic algorithms. These new hybrid algorithms can speed up the global convergence rate without losing the strong robustness of the original algorithms. The main goal is to speed up the algorithm convergence and therefore to provide a more efficient tool for a wider range of practical applications while preserving the attractive characteristics of the original meta-heuristic algorithms. Additionally, these swarm intelligence algorithms are compared individually. In this regard, the framework of the presented algorithms is explained. First of all, the encoding scheme, initialization, and VNS as a joint section of the structure of the suggested algorithm are qualified. Next, the presented algorithms are described.

7.1. Encoding scheme and initialization

The Random-Key (RK) technique is employed in order to enable the developed hybrid meta-heuristic algorithms and to decompose the primary solution to solve the proposed problem as an encoding process. Then, the sub-solutions are divided into two sorts in the developed problem:

- *The first encoding scheme:* Choice sub-solution is utilized to specify established DCs. Further, firstly, by using uniform distribution $U(0, 1)$ is generated a matrix with $|W|$ elements. Hence, the first Max W units are chosen with the biggest values as established DCs. For example, the encoded solution $\{0.58, 0.03, 0.71, 0.93, 0.37\}$ with $W_{max} = 4$ displays the decomposed solution $\{1, 0, 1, 1, 0\}$.
- *The second encoding scheme:* the allocation sub-solution provides to allocate the laboratories to the permanent centers. As indicated in Fig. 6, a vector $\max(1 \times (g_{max} + |i| - 1))$ with a uniform distribution between $U(0, 1)$ has been generated. In this regard, this matrix as a permutation matrix is decomposed that it indicates the degree of each value. Then, numbers more than $|g_{max}|$ show laboratory symptoms and less than $|g_{max}|$ indicate permanent centers that are considered in the permutation matrix. The laboratory symptoms are utilized as dividers that display various permanent centers. Thus, the string of permanent centers (PCs) among dividers proofs the sequence of points that a laboratory must be allocated.

In terms of population, in order to generate a sample of $PopSize$ particles is used the initialization procedure. According to the M -dimensional hyperspace known as the feasible region, the particles are randomly generated. Dimensions show sub-solutions while the mentioned above is explained. Based on the uniform distribution (u_m, l_m), the value of initial is generated as follows:

$$y_m^j = l_m + \sigma(u_m - l_m) \tag{42}$$

$\forall m \in \{1, 2, \dots, M\}, j \in \{1, 2, \dots, mPop\}, \sigma \sim U(0, 1)$

where u_m and l_m are the lower and upper bounds in each dimension, respectively. RK scheme is executed to find the corresponding values of the initial solutions in the discrete area after generating the particles. Eventually, these particle values are assessed to compute the objective function.

7.2. Variable neighborhood search algorithm

In this sub-section, the neighborhood structure (NS) of the VNS algorithm in the search process in order to optimize problems is using a series of systematic changes. VNS is considered as a famed local search algorithm due to its performance and efficiency to solve various optimization problems (Fakhrzad and Goodarzian, 2019). A complete process of the VNS algorithm is able to found in Lu et al. (2020). VNS has been successfully employed in different optimization problems in supply chain management fields such as cross-docking (Ranjbar

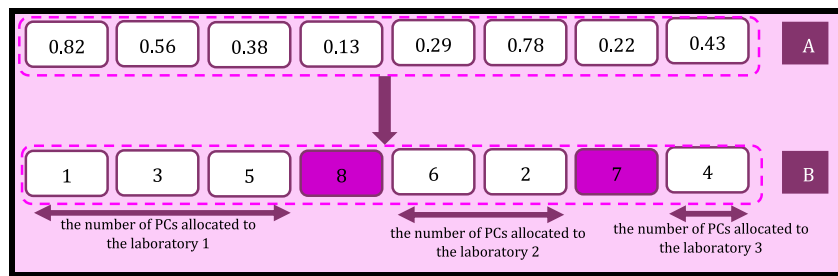


Fig. 6. The illustration of a schematic of the encoding process based on allocation permanent center to laboratory ($g_{max} = 6, i = 3$).

```

VNS Procedure ()
Initialization
Set parameters ( $nPop$ , maximum number of iteration( $Maxit$ ))
Consider a set of neighborhood structures  $N_{ns}(ns = 1, 2, \dots, ns_{max})$ 
Receive/generate population with size  $nPop$  and assess them
Pick up the best solution as initial solutions  $S^*$ ;
For  $itr=1$  to  $Maxit$  do//main loop
    For  $N_{ns} = 1$  to  $ns_{max}$  do
         $S \leftarrow S^*$ ;
        Determine a random solution  $S'$  from  $N_{ns}$ // shaking
        Perform a neighborhood search  $N_{ns}$  on  $S'$  to find  $S''$ 
        Evaluate  $S''$ ;
        If  $f(S'') < f(S^*)$ 
             $S^* \leftarrow S''$  and break;
        Else if  $f(S'') = f(S^*)$ 
            Select one of them randomly;
        End if
    End for
Report  $S^*$ ;
End
    
```

Fig. 7. The pseudo-code of the VNS algorithm.

and Saber, 2020), allocation–location (Abbassi et al., 2020), inventory control, and network design (Kuo et al., 2020), and distribution–production problems (Tayebi-Araghi et al., 2020). VNS starts with an initialization procedure, while indicates in Fig. 7. where ns_{max} illustrates the maximum number of NSs with determined sequence and N_{ns} ($ns = 1, 2, \dots, ns_{max}$) shows a set of NSs symbolized that it is utilized to attain the near-optimal solution.

7.3. HACO-VNS algorithm

The ACO introduced by Dorigo and Di Caro (1999) for the first time, which is a famous meta-heuristic algorithm in swarm intelligence-based algorithms. The ACO was used successfully to solve the problems in various areas containing vehicle routing problem (Li et al., 2019), supply chain network (Fakhrzad and Goodarzian, 2020), scheduling problem and inventory control (Bottani et al., 2019), and healthcare management (Decerle et al., 2019). For more details about the ACO algorithm, scholars can be found in Mohammed and Duffuaa (2020). In order for the best solution achieved from the main loop in each iteration, VNS is considered as a local search approach applied in hybrid proposed meta-heuristic algorithms. Fig. 8 shows the steps of HACO-VNS algorithm.

7.4. HFSA-VNS algorithm

The FSA is a new intelligent swarm approach by the natural feeding behavior of fish that this algorithm first developed by Li (2002) that

includes following, searching, and swarming behaviors. FSA is a new method that has been successfully employed in network design, supply chain systems, and location, allocation, inventory problems (Tian et al., 2020). In this algorithm, the satisfaction of food for the fish is demonstrated as FS_i , and a fish is indicated by its D -dimensional position $X_i = (x_1, x_2, \dots, x_k, \dots, x_D)$. In this regard, the communication among two fish is represented by their Euclidean distance $d_{ij} = \|x_i - x_j\|$. The parameters of FSA consist n (the size of the fish population), step (maximum step length), δ (a crowd factor), and visual (representing the visual distances of fish). According to the three distinct behaviors include (i) Searching behavior, (ii) Swarming behavior, and (iii) Following behavior, all fish effort to identify locations able to satisfy their food. Eventually, in the main loop, the VNS is represented on the obtained best solution. Then, for more details about the FSA algorithm, researchers can refer to Tian et al. (2020). The pseudo-code of the general scheme of the HFSA-VNS algorithm is indicated in Fig. 9.

7.5. HFA-VNS algorithm

Firefly algorithm (FA) is one of the algorithms derived from nature that simulates the social behavior of fireflies. This algorithm was introduced by Yang (2010). Fireflies produce lights that have different light patterns of each from the other. They use this light in order to attract pairs and prey, the amount of this light is directly related to the attractiveness of fireflies. By considering the amount of light of each firefly as the value of the objective function, the behavior of the

```

HACO-VNS Procedure ()
Step 1: initialization
  %Set parameters (MaxIt(Maximum Number of Iteration),
  nAnt(Number of Ants or Population Size), IPh (Initial Pheromone),
  alpha (Pheromone Exponential Weight), Beta (Heuristic Exponential Weight),
  and ER (Evaporation Rate)).
  %Generate initial ants randomly and assess them.

While (hasn't met stop condition (MaxIt) ) do

  Step 2: ACO main loop
  Step 3: Move Ants ()
  Step 4: Update Pheromones ()
  Step 5: Evaporation ()
  Step 6: Store Best Cost ()
  Step 7: Show Iteration Information ()
  Step 8: VNS local search ()

End while
End

```

Fig. 8. The pseudo-code of the HACO-VNS algorithm.

```

HFSA-VNS Procedure ()
Step 1: initialize all fishes
  %Set parameters (consist n (the size of the fish population),
  step (maximum step length),  $\delta$  (a crowd factor),
  and visual (v= representing the visual distances of fish)).

While (Not termination-condition) do

  Step 2: Swarming behavior ()
  Step 3: Following behavior ()
  Step 4: Searching behavior ()
  Step 4: Implement the better of two behaviors on every fishes ()
  Step 5: VNS local search ()
  Step 6: Final solution ()

End while
End

```

Fig. 9. The pseudo-code of the HFSA-VNS algorithm.

fireflies can be modeled as an optimization algorithm. The modeling process has three basic assumptions: (i) Fireflies are all unisexual; (ii) The amount of attractiveness between two fireflies is directly relevant to their brightness and is inversely relevant to the distance between them; (iii) The brightness of fireflies is determined based on the amount of the associated objective functions with them (Yang, 2010).

As mentioned, the attractiveness of fireflies (β) is relative and depends on the distance between the two fireflies (r) and light attractiveness coefficient (γ), which is calculated as follows:

$$\beta_{(r)} = \beta_0 e^{-\gamma r^2} \quad (43)$$

where β_0 , the attractiveness of the brighter firefly is at $r = 0$. The position of firefly i th after moving to firefly j th, which is brighter, is calculated based on Eqs. (44) and (45) as follows:

$$x_i^n = x_i^{n-1} + \beta_0 e^{-\gamma r_{ij}^2} (x_j^{n-1} - x_i^{n-1}) + \alpha e_i^{n-1} \quad (44)$$

$$r_{ij} = \|x_i - x_j\| \quad (45)$$

where x_i shows the position of the less dim firefly, x_j indicates the position of the brighter firefly, n states the iteration number, α is a random number, and e_i^{n-1} is a vector of random numbers that can have a uniform or Gaussian distribution. The attraction of fireflies continues until they are absorbed into the available brightest firefly, in fact,

this firefly generates the best value for our objective function. VNS is considered as a local search method, which is employed in hybrid suggested meta-heuristic algorithms to the best solution achieved from the main loop in each iteration. Therefore, the steps/pseudo-code of the HFA-VNS algorithm is indicated in Fig. 10.

8. Computational experiments

First of all, the data generation process is described in order to evaluate the efficiency of the suggested algorithms. Hence, the parameter tuning methodology and assessment metrics are explained. Next, the obtained outcomes by suggested algorithms (HACO-VNS, HFSA-VNS, and HFA-VNC) are compared and analyzed based on various assessment metrics. In this regard, the suggested algorithms are evaluated according to the attained Pareto front. Finally, to validate the SSMSCN model, a set of sensitivity analyses and a real case study are used to evaluate. The proposed algorithms were implemented in MATLAB® 2020b software on a PC with 6 GHz RAM.

8.1. Examples of experimental problems

To evaluate and compare the suggested methods, a numerical test was designed in this paper. Hence, the existing benchmarks in the examined literature are not available for the SSMSCN problem during the

```

HFA-VNS Procedure ()
Step 1: initialize all fishes
    %Set parameters (consist MaxIt (Maximum Number of Iterations),
    nPop (Number of Fireflies (Swarm Size)), gamma (Light Absorption Coefficient),
    beta (Attraction Coefficient Base Value), alpha (Mutation Coefficient),
    alpha_damp (Mutation Coefficient Damping Ratio), and delta (Uniform Mutation Range)

While (Not termination-condition) do

Step 2: Empty Firefly Structure ()
Step 3: Initialize Population Array ()
Step 4: Initialize Best Solution Ever Found ()
Step 4: Create Initial Fireflies ()
Step 5: Array to Hold Best Cost Values ()
Step 6: Store Best Cost Ever Found ()
Step 7: Show Iteration Information ()
Step 8: Damp Mutation Coefficient ()
Step 9: VNS local search ()

End while
End
    
```

Fig. 10. The pseudo-code of the HFA-VNS algorithm.

Table 2
The samples of the experiment problems.

Categorization	Sample	<i>h</i>	<i>g</i>	<i>i</i>	<i>w</i>	<i>m, m'</i>	<i>e, r, t</i>
Small	S1	2	1	2	1	4	1,1,1
	S2	3	2	2	2	4	2,2,3
	S3	3	3	2	2	6	2,3,4
	S4	4	3	3	3	6	2,3,4
Medium	M5	8	6	4	4	12	4,4,6
	M6	10	8	6	5	14	4,5,6
	M7	10	10	6	5	20	5,5,7
	M8	12	12	8	8	28	5,6,7
Large	L9	18	14	12	10	34	6,7,8
	L10	22	16	16	10	64	7,8,8
	L11	30	18	20	12	84	8,9,10
	L12	36	22	22	14	120	9,10,10

Table 3
The range of the proposed parameters (\$ = dollars, S = seconds).

Parameters	Range	Parameters	Range	Parameters	Range
<i>em_{wl}</i>	U(1, 5)	<i>rw_w</i>	U(0.1, 0.7)	<i>ct_{gwm}</i>	U(15, 55)\$
<i>cr_m</i>	U(2, 6)	<i>Bd_g</i>	U(100,2000)\$	<i>cs_{w_{wl}}</i>	U(100,400)\$
<i>ma_{ml}</i>	U(2, 16)	<i>ew_w</i>	U(50, 250)\$	<i>cou_{wl}</i>	U(30,80)\$
<i>ma_{mw}</i>	U(5, 30)	<i>rd_w</i>	U(20, 40)	<i>f_{gm}</i>	U(15,35)\$
<i>vol_{mw}</i>	U(500,8000)	<i>ps_{h_{mh}}</i>	U(1, 5)	<i>pc_{mit}</i>	U(50, 180)\$
<i>vol_w</i>	U(100,6000)	<i>ps_{u_{mh}}</i>	U(5, 10)	<i>pr_{mh}</i>	U(0.2,0.5)
<i>nf_w</i>	U(2, 20)	<i>s_{mh}</i>	U(5, 10)	<i>d_{hmt}</i>	U(100, 500)
<i>nv_w</i>	U(5, 50)	<i>c_{p_{gm}}</i>	U(100,5000)	<i>j_m</i>	U(10, 120)\$
<i>we</i>	U(0.1, 0.6)	<i>cw_{w' m}</i>	U(25, 60)\$		
<i>we'</i>	U(0.2, 0.8)	<i>cw_{w_{hm}}</i>	U(20, 40)\$		

COVID-19 pandemic and different instances are required to design the experiment problems. Along the way, the test problems are categorized into three scales: small, medium, and large. In this regard, a numerical test of problems in various scales contains hospital (*h*), permanent center (*g*), the medicine production laboratory (*i*), the location of the established distribution center (*w*), medicines (*m* and *m'*), the period of shipping medicine (*e*), the period of medicine production (*r*), and the periods (*t*) is reported in Table 2. Additionally, the range of parameters is provided in Table 3.

8.2. Assessment metrics

In this subsection, various efficiency evaluation metrics are employed to quantitatively compare the quality of attained Pareto front

and non-dominated solutions by the mentioned above algorithms. Hence, different efficiency metrics should be used simultaneously, according to the incommensurable nature and confliction of measures in evaluating the quality of approximate Pareto sets (Goodarzian et al., 2020a). Along the way, six assessment metrics are employed as follows:

- Hyper Volume (HV) (Van Veldhuizen and Lamont, 1999),
- Number of Pareto Solution (NPS) (Sahebjamnia et al., 2020; Goodarzian et al., 2020a),
- Mean Ideal Distance (MID) (Goodarzian et al., 2020a),
- Maximum Spread (MS) (Goodarzian et al., 2020a),
- Inverted Generational Distance (IGD) (Zhang et al., 2009),
- Spread of Non-Dominance Solution (SNS) (Goodarzian et al., 2020a).

8.3. Parameters setting: response surface method

In some situations, parameter tuning plays such a crucial role in meta-heuristics efficiency, which is an important phase in the proposed meta-heuristic algorithms. In order to run the algorithm to achieve the input parameters, a parameter setting process should be performed. In this study, the response surface method (RSM) as a proper approach utilized in types of parameter tuning and industrial problems is employed, while it was introduced by Box and Wilson (1951) for the first time. The presented levels along with the number of them for each test and the parameters tuning are reported in

Tables 4 and 5, respectively. The tuned parameters of all proposed meta-heuristics in problem 7 are evaluated in order to have a suitable comparing.

In order to the efficiency of the proposed algorithms, various assessment metrics are utilized in this paper. According to all the six assessment metrics, a choice problem is organized to set input parameters that lead to a multi-objective decision-making problem. In this regard, the utility function is provided as follows (Box and Wilson, 1951):

$$B = \sqrt[Z]{b_1 (x_1)^{Z_1} \times b_2 (x_2)^{Z_2} \times \dots \times b_l (x_l)^{Z_l}} \quad (46)$$

where, *Z* indicates the severity of *b_j(x_j)* utilized to confirm on the lower/upper bounds and *b_j(x_j)* shows the normalized utility functions of *x_j*, while if *Z* is between 1 and 10, more important is performed on the aims. Next, parameters *Z* for IGD, SNS, MS, MID, NPS, and HV are

Table 4
The levels of the algorithms factors along with their number of tests.

Algorithms	No. Tests Total No. (n_f, n_{ax}, n_{cp})	Factors and their levels						
		Upper limit (+), Lower limit (-)						
HACO-VNS	82 = ($2^6, 12, 6$)	<i>MaxIt</i> (-, +) (100, 400)	<i>nAnt</i> (-, +) (65, 200)	<i>I Ph</i> (-, +) (10, 50)	<i>alpha</i> (-, +) (0.1, 0.6)	<i>Beta</i> (-, +) (0.2, 0.8)	<i>ER</i> (-, +) (0.25, 0.7)	
HFSA-VNS	30 = ($2^4, 8, 6$)	<i>n</i> (-, +) (100, 400)	<i>step</i> (-, +) (65, 200)	<i>delta</i> (-, +) (10, 50)	<i>v</i> (-, +) (0.1, 0.6)			
HFA-VNS	104 = ($2^7, 14, 6$)	<i>MaxIt</i> (-, +) (100, 400)	<i>nPop</i> (-, +) (65, 200)	<i>gamma</i> (-, +) (0.1, 0.5)	<i>alpha</i> (-, +) (0.1, 0.6)	<i>Beta</i> (-, +) (0.2, 0.8)	<i>delta</i> (-, +) (0.3, 0.7)	<i>alpha - damp</i> (-, +) (0.1, 0.9)

Table 5
Desirability (B), parameters tuning, R-squared (R^2).

Algorithms	Parameters tuning	R^2 B	R^2 IGD	R^2 SNS	R^2 MS	R^2 MID	R^2 NPS	R^2 HV
HACO-VNS	<i>MaxIt</i> = 200, <i>nAnt</i> = 100, <i>I Ph</i> = 25, <i>alpha</i> = 0.35, <i>Beta</i> = 0.45, <i>ER</i> = 0.3	0.766	69%	66%	62%	63%	61%	71%
HFSA-VNS	<i>n</i> = 150, <i>step</i> = 95, <i>delta</i> = 35, <i>v</i> = 0.5,	0.632	61%	63%	56%	57%	54%	65%
HFA-VNS	<i>MaxIt</i> = 250, <i>nPop</i> = 150, <i>gamma</i> = 0.5, <i>alpha</i> = 0.4, <i>Beta</i> = 0.75, <i>delta</i> = 0.55, <i>alpha - damp</i> = 0.32	0.667	63%	65%	57%	59%	58%	67%

Table 6
The outputs of the evaluation metric of the developed meta-heuristic algorithms.

Assessment metrics	Sample	HACO-VNS	HFSA-VNS	HFA-VNS	Assessment metrics	Sample	HACO-VNS	HFSA-VNS	HFA-VNS
IGD	S1	0.044	0.038	0.041	SNS	S1	3182	3455	3271
	S2	0.045	0.039	0.042		S2	3345	3678	3472
	S3	0.047	0.041	0.045		S3	3403	3681	3567
	S4	0.048	0.042	0.046		S4	3562	3702	3601
	M5	0.049	0.044	0.048		M5	3877	4012	3987
	M6	0.051	0.045	0.050		M6	3946	4309	4128
	M7	0.052	0.046	0.051		M7	4126	4791	4567
	M8	0.058	0.047	0.053		M8	4780	5023	4981
	L9	0.063	0.051	0.054		L9	5136	5699	5267
	L10	0.069	0.053	0.059		L10	5346	5823	5671
	L11	0.074	0.057	0.065		L11	5802	6126	5987
	L12	0.079	0.061	0.069		L12	6245	6802	6452
MS	S1	4256	4432	4356	MID	S1	4.65	1.35	3.78
	S2	4358	4467	4378		S2	4.92	1.76	3.82
	S3	4491	4671	4581		S3	5.32	2.04	4.12
	S4	4503	4783	4672		S4	5.81	2.67	4.28
	M5	4692	4981	4823		M5	6.45	2.93	4.56
	M6	4893	5134	4902		M6	6.81	3.14	4.89
	M7	4906	5349	5034		M7	6.97	3.54	5.13
	M8	5134	5677	5239		M8	7.04	3.82	5.29
	L9	5467	5982	5512		L9	7.16	4.53	5.89
	L10	5789	6322	5938		L10	7.45	4.78	6.25
	L11	5903	6458	6123		L11	7.68	4.95	6.39
	L12	6278	6577	6344		L12	7.96	5.12	6.89
NPS	S1	2	4	3	HV	S1	2.67	3.51	2.98
	S2	2	4	3		S2	2.83	3.72	3.02
	S3	3	5	4		S3	2.94	4.56	3.45
	S4	4	6	5		S4	3.04	5.78	3.78
	M5	5	7	6		M5	3.42	6.23	4.56
	M6	4	6	5		M6	3.78	6.58	5.38
	M7	4	6	5		M7	3.95	7.04	6.77
	M8	5	8	7		M8	4.12	7.25	6.81
	L9	6	9	8		L9	4.67	7.87	7.34
	L10	6	8	7		L10	5.98	8.54	7.94
	L11	8	10	9		L11	6.52	8.92	8.35
	L12	9	12	11		L12	7.61	9.21	8.72

equal to 1, 1, 1, 2, 2, and 3 according to their remarkable significance is set in this paper, respectively.

where $n_f = 2^k$, k shows variables and a lower bound and an upper bound for each variable and there are (2k) a fraction or tests of it. n_{cp} and n_{ax} indicate central points and axial points (2k) (face centered) in this study, respectively.

8.4. Comparison of the proposed algorithms: Pareto optimal analysis

In this paper, in order to compare the effectiveness of algorithms, six assessment metrics are used. Firstly, according to the attained Pareto front for all the test problems, the assessment metrics are computed to evaluate the performance of each method, while are provided in Table 6.

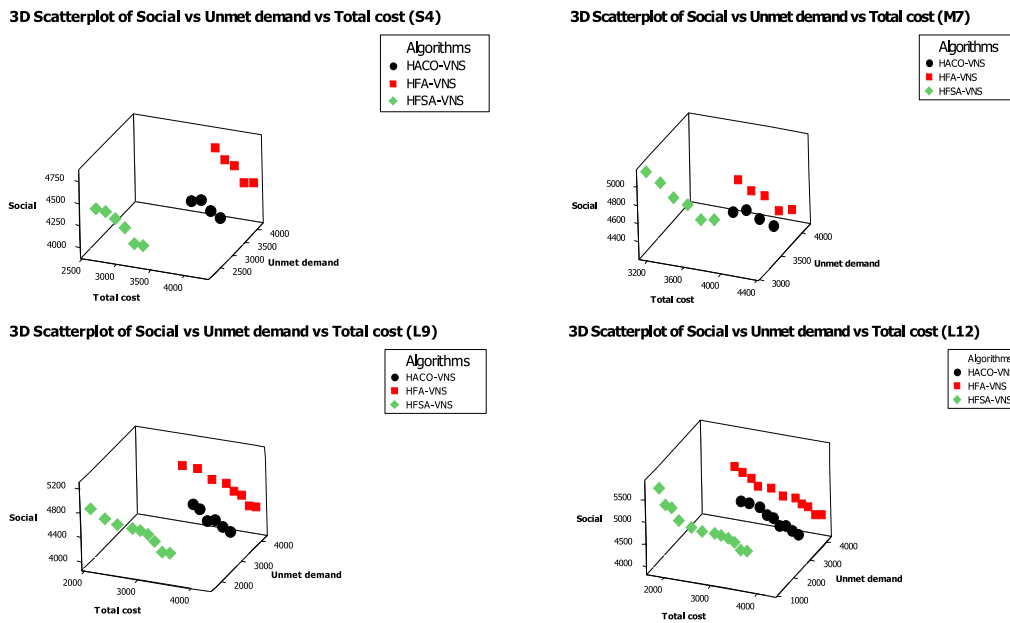


Fig. 11. Pareto frontier of suggested algorithms in S4, M7, L9, and L12.

Therefore, a sample of non-dominated solutions of suggested algorithms in four experiment problems (S4, M7, L9, and L12) is presented in Fig. 11. It is clear that HFSA-VNS indicates the best efficiency, while HACO-VNS illustrates the worst performance.

Further, a set of statistical comparisons between the suggested algorithms according to the Pareto optimal analyses taken by measurement metrics is conducted to find out the best methods in this work. According to the reported outcomes in Table 6 are converted to a popular metric called Relative Deviation Index (RDI) (Goodarzian et al., 2020a) that it is formulated in Eq. (47).

$$RDI = \frac{|Alg_{sol} - Best_{sol}|}{Max_{sol} - Min_{sol}} \times 100 \quad (47)$$

where Max_{sol} and Min_{sol} display the maximum and the minimum values between all values resulted from methods, $Best_{sol}$ shows the best solution between algorithms, and Alg_{sol} indicates the obtained objective value by a given measurement metric of the method. Accordingly, the means plot and Least Significant Difference (LSD) for the presented algorithms have been provided. The outcomes run by Minitab 18. 1 statistical software are depicted in Fig. 12.

As a result, in all assessment metrics, based on the results reported in Fig. 12 and Table 6, the HFSA-VNS algorithm has more robust than two other of the proposed algorithms, but the HACO-VNS has the worst performance than HFSA-VNS and HFA-VNS. It is clear that a lower value of RDI brings a higher quality of algorithms.

8.5. Case study to validate the SSMSCN model during COVID-19 pandemic

Tehran is the most populous city in Iran and the capital of this country. The management of the medicine SSCN in this city has always been one of the concerns of decision-makers in the COVID-19 pandemic condition. Therefore, in this study, in order to test the proposed model of medicine SSCN in Tehran\Iran is examined. As shown in Fig. 13, in the case study, ten hospitals, five medicine production laboratories, five permanent centers, and 6 distribution centers were considered. Likewise, collected data obtained during the period 1.08.2020 to 1.01.2020, while the place of data collection was in Tehran City/Iran Country. The gathered information obtained through reliable sources including Google Maps, information from the hospitals, laboratories, and the Ministry of Health. In addition, the information about transportation cost is calculated from Google Maps. Thus, each unit of distance is

Table 7

The medicine transportation cost between permanent centers and distribution centers (dollars).

Permanent centers	Medicine type	Distribution centers					
		Moniriye	Dibaji	Sabalan	Ferdowsi	Pirozi	Poonak
Gheydariye	Type 1	9	5	16	16	19	15
	Type 2	5	6	10	13	20	14
	Type 3	9	17	20	5	6	5
Vanak	Type 1	17	7	6	10	12	7
	Type 2	9	10	7	5	18	7
	Type 3	17	10	12	13	19	13
Majidiye	Type 1	9	9	17	7	9	11
	Type 2	6	13	13	8	19	12
	Type 3	19	5	6	19	16	19
Narmak	Type 1	12	10	19	11	7	20
	Type 2	8	12	10	7	19	12
	Type 3	11	18	5	15	8	13
Enghelab	Type 1	18	6	12	8	18	7
	Type 2	11	16	13	12	7	14
	Type 3	9	17	16	7	8	10

considered equal to 1 unit of cost. The way it works is that 1 km of distance is equal to one unit of cost. Information related to the importance of medicines was extracted from each hospital based on the type of patient needs. Also, the information related to the released co2 cost from the Environment Organization is determined based on the type of established center and the type of used vehicle.

Table 7 shows the medicine transportation cost between permanent centers and distribution centers in dollars. As it turns out, there are three types of medicines to transfer between permanent centers and distribution centers.

Table 8 reports the amount of demand and the importance of medicines in each hospital. For example, the demand for type 1 medicine in Taleghani Hospital is 358 kg and the importance of this medicine is 0.25. Table 9 shows the establishment costs, operating costs, and fixed created jobs at the location of the distribution center according to the capacity level of the distribution centers.

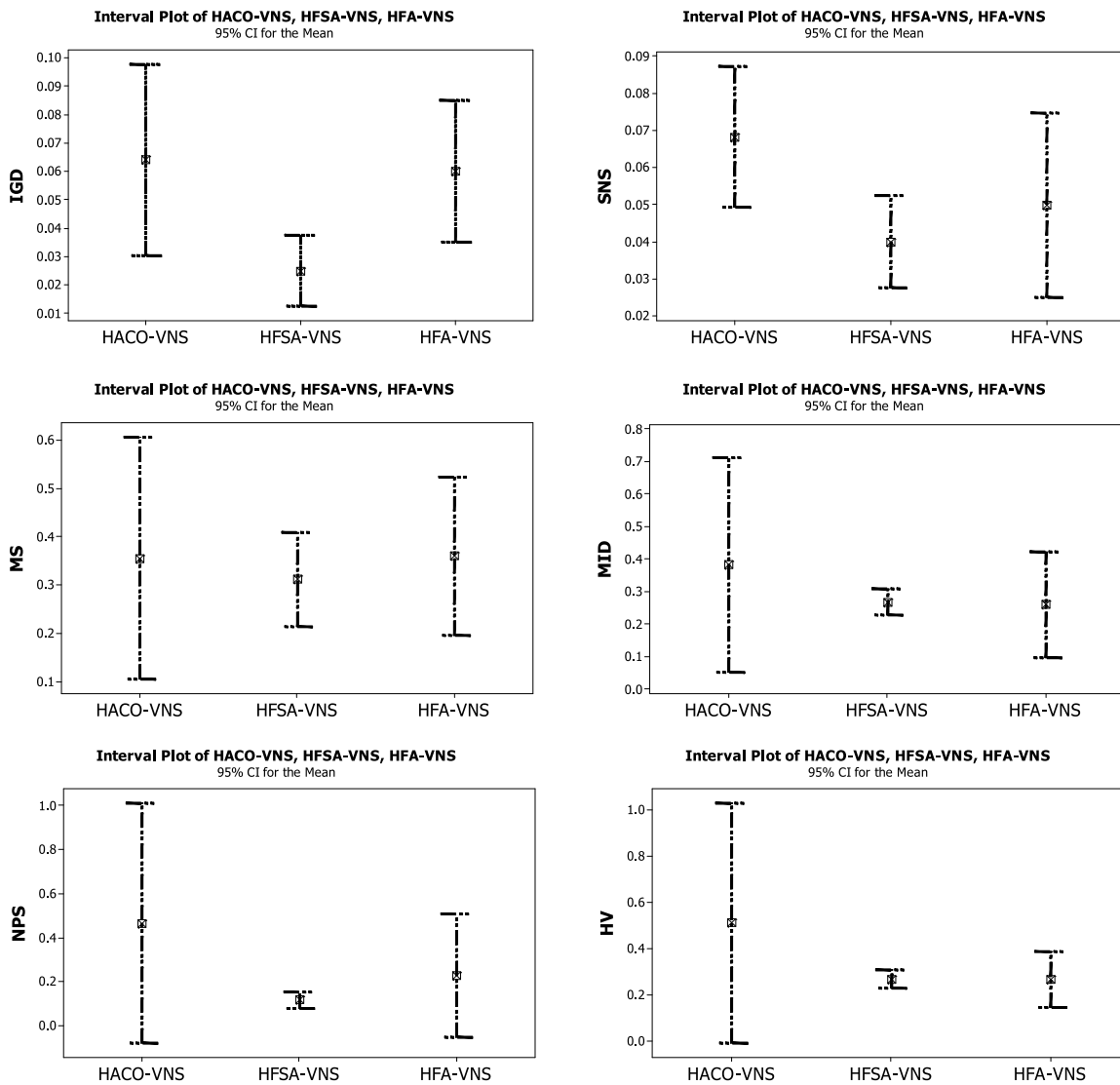


Fig. 12. Means plot and LSD intervals for the proposed algorithms in all assessment metrics.

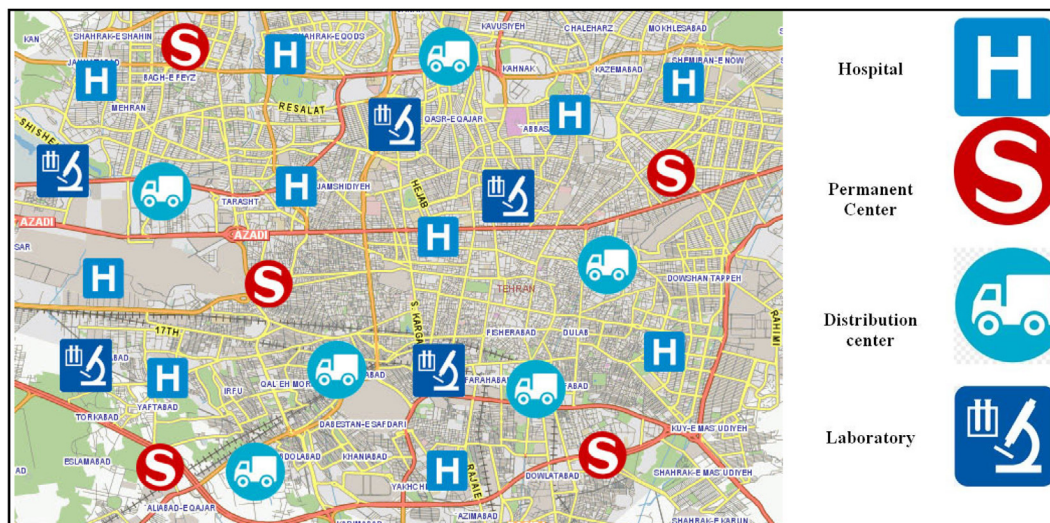


Fig. 13. The case study map.

Table 8
The amount of demand and importance of medicines in each hospital.

Hospital/Medicine demand/importance	Taleghani	Nikan	Nour	Sina	Jam	Besat	Fajr	Kasra	Gandi	Arash
Type 1	358	251	351	247	245	229	242	247	431	438
Importance	0.25	0.20	0.30	0.30	0.35	0.10	0.40	0.20	0.35	0.25
Type 2	299	293	218	380	488	386	399	422	348	416
Importance	0.50	0.45	0.40	0.50	0.35	0.60	0.40	0.50	0.30	0.50
Type 3	499	426	355	418	236	359	451	343	263	435
Importance	0.25	0.35	0.30	0.20	0.30	0.30	0.20	0.30	0.35	0.25

Table 9
The establishment costs, operating costs, and fixed created jobs (dollars).

Parameters	Capacity level	Distribution centers					
		Moniriye	Dibaji	Sabalan	Ferdowsi	Pirozi	Poonak
Establishment cost	Small	700000	600000	550000	900000	600000	800000
	Medium	1500000	1100000	1000000	1200000	1000000	1400000
	Large	2300000	2500000	2000000	2500000	2000000	2100000
Operation cost	Small	14000	15000	20000	10000	15000	10000
	Medium	25000	20000	25000	20000	20000	25000
	Large	35000	30000	30000	25000	25000	30000
Fixed created jobs	Small	15	13	11	10	12	10
	Medium	55	30	40	50	45	35
	Large	100	70	70	80	50	60

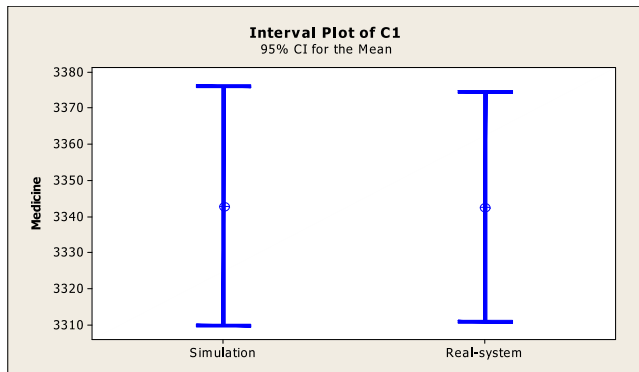


Fig. 14. A 95% confidence interval for results obtained by simulation and real system.

8.6. Case study results

In this paper, the amount of required medicine for the 4 distribution functions Loglogistic, Lognormal, Weibull, and Normal were explored. As evident, the correlation coefficients for the mentioned distribution functions are 0.977, 0.986, 0.985, and 0.995, respectively. Therefore, the distribution function of required medicine for COVID-19 patients follows the Normal distribution function with an average of 3325.14 and a variance of 136.2.

Along the way, Fig. 14 shows the results of comparing the estimated amount of medicine with the real world. In order to validate the simulation model, the model was run 100 times and the average performance were considered. As evident in Fig. 14, the average amount of estimated medicines at the 95% confidence level is a good estimate of the real world and the proposed simulation model can be trusted.

Further, Fig. 14 shows the result of the hypothesis test $H_0 : \mu = \mu_0$ versus $H_1 : \mu \neq \mu_0$. The value of μ_0 is called the expected value of the estimated parameter. Additionally, the value of μ represents that value taken from the real-world. The obtained P -value is greater than 0.05 and the null hypothesis is not rejected. Hence, it can be concluded that the average demand calculated by a 95% confidence interval follows the real-world average.

Table 10 demonstrates the allocation of hospitals to distribution centers. Values 1 and 0 indicate allocation and non-allocation, respectively. As can be seen, for example, Taleghani Hospital has been

Table 10
The allocation of hospitals to distribution centers.

Hospital/ Distribution center	Taleghani	Nikan	Nour	Sina	Jam	Besat	Fajr	Kasra	Gandi	Arash
Moniriye	1	0	1	0	1	1	0	0	0	1
Dibaji	0	1	1	0	0	1	1	1	0	0
Sabalan	1	0	1	1	0	1	0	1	0	1
Ferdowsi	0	0	1	0	1	1	1	1	1	0
Poonak	1	0	0	0	1	0	0	0	0	0

Table 11
Medicine flow between laboratory and permanent center (Kg).

Permanent centers	Medicine type	Distribution centers				
		Gheytariye	Vanak	Majidiye	Narmak	Enghelab
Laboratory 1	Type 1	113	-	124	162	178
	Type 2	149	-	198	159	124
	Type 3	159	-	130	196	206
Laboratory 2	Type 1	113	176	92	191	114
	Type 2	155	204	195	208	138
	Type 3	173	109	227	136	196
Laboratory 3	Type 1	204	95	-	202	192
	Type 2	133	146	-	195	223
	Type 3	218	226	-	168	209
Laboratory 4	Type 1	-	106	109	134	169
	Type 2	-	125	270	155	190
	Type 3	-	108	155	159	228
Laboratory 5	Type 1	118	68	139	-	145
	Type 2	151	165	136	-	179
	Type 3	204	174	168	-	201

allocated to Moniriye, Sabalan, Pirozi, and Poonak distribution centers. In this table, the Pirozi Distribution Center, which was designated as the Candidate Distribution Center, has not been established and only 5 distribution centers out of 6 possible centers have been established. In addition, the flow of medicines between laboratories and temporary centers in kilograms is shown in Table 11. As it is clear that, for instance, the amount of flow from laboratory 1 to the Vanak distribution center for the three types of medicines is 124, 198, and 130 kg, respectively. Table 12 reports the number of medicine shortages in each hospital in kilograms.

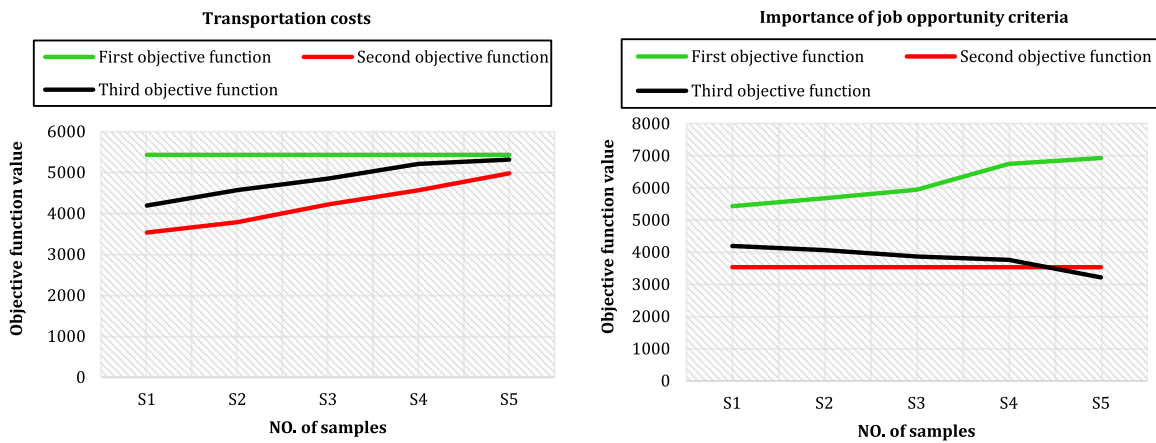


Fig. 15. The results of the sensitivity analysis of transportation cost and job opportunity criteria.

Table 12
The amount of medicine shortage in hospital (Kg).

Hospital/ Distribution center	Taleghani	Nikan	Nour	Sina	Jam	Besat	Fajr	Kasra	Gandi	Arash
Type 1	0	24	0	0	13	0	34	0	0	29
Type 2	11	0	0	16	0	0	0	21	0	0
Type 3	15	0	0	0	0	0	10	0	20	0

8.7. Sensitivity analysis

A set of sensitivity analyses has been carried out on the significant parameters to recognize the behavior of the case study. In this study, the HFSA-VNS algorithm is the most performed algorithm that is considered to handle the SMSCN problem. Transportation costs (cu'_{wm} , cu'_{whm} , ct'_{gum}), the importance of job opportunity criteria (we), demand (d'_{hmt}), storage capacity of medicine in permanent center and distribution center (cp'_{gm} , vol'_{mw}), released CO₂ cost parameters (em'_{wl} , cr'_m) and the volume of one unit of medicine (vol'_{ml}) are a set of changes for analysis. Each analysis is divided into numbered five samples as S1–S5. Eventually, all outputs are reported in Table 13.

According to Table 13 and Fig. 15, increasing transportation costs cause to keep social factors constant and fixed. Also, increasing transportation costs increases the costs of the total supply chain network and also the amount of unsatisfied demand. Raised the importance of job opportunity criteria raises job creation. Raised this coefficient from 0.3 to 0.95 raises the first objective function from 5432 to 6931 units. Higher employment reduces unsatisfied demand. Also, raising this coefficient, the supply chain costs keep fixed and without change.

As evident in Fig. 16, enhanced amount of demand enhances the social aspects of the sustainability supply chain network including job creation. It is clear that more labor is needed to handle more demand. Also, increased demand increases supply chain costs. In this case, the slope of cost increases is high. Then, increasing the amount of demand from 3346 to 3896 units leads to an increase in costs from 39740 to 48750 units. Finally, the increase in demand due to the stability of other parameters involving the capacity of the centers will increase unsatisfied demand.

Increasing the storage capacity of medicine in a permanent center and distribution center will cause to increase employment. The slope of increasing the amount of job creation is very low while increasing the capacity of permanent centers and distribution centers decreases the amount of supply chain costs. The reason for this is that by raising the capacity of distribution centers, the number of established distribution centers decreases, and the costs of establishing a new center are saved. Additionally, enhanced the capacity of the centers reduces the amount of unsatisfied demand. For instance, by enhancing the capacity from

500 to 4000 units, the amount of unsatisfied demand decreases from 4193 to 3217 units.

As illustrated in Fig. 17, increasing the amount of released CO₂ during the establishment of distribution centers and transportation of medicines causes social effects remain fixed and without change. Raising this parameter greatly increases the amount of supply chain costs due to more environmental pollution. Increasing the amount of released CO₂ also has no effect on the amount of unsatisfied demand, and this objective function remains almost constant as the amount of CO₂ increases.

Thus, enhanced the volume of one unit of medicine enhances job creation and the total costs because of the increase in the number of transportation systems and in the number of established centers. For example, by increasing the volume of medicines from 0.5 to 1.5 units, costs grow from 3678 to 4971 units. Therefore, it is recommended for reducing the total costs, medicines should be supplied in smaller packages. Eventually, raised the volume of medicines increases the amount of unsatisfied demand because it requires more vehicles, labor, and distribution centers.

8.8. What-If analysis

The simulation results are analyzed by using "What-if "analysis, which is a data-intensive simulation whose goal is to inspect the behavior of a complex system such as the outbreak of the COVID-19 pandemic under some given scenarios. Table 14 reports the used parameters and variables in the simulation. The contact rate has been considered equal to 60 people. This means that each patient person can infect another 60 people. The number of susceptible people is equal to 718,000 and the mortality rate is estimated at 4% according to the World Health Organization. The course of the disease, the diagnosis rate, and the recovery rate of COVID-19 are equal to 14 days, 40%, and 90%, respectively.

Table 15 represents the results of the What-If analysis that six scenarios consider for this analysis. In each scenario, one of the effective parameters on the COVID-19 pandemic outbreak will change and its effect on the estimated demand values will be measured. Reducing the contact rate by up to 30% causes reduces the amount of demand by up to 63% and increasing the contact rate by up to 30% causes increases the demand by up to 57%. Moreover, it is clear that the contact rate will greatly affect the number of required medicines. Therefore, keeping social distance and quarantine is recommended to reduce the contact rate. Also, increasing the number of talented people by up to 10% causes increases the amount of required demand by up to 23%. Moreover, it is necessary to pay more attention to talented people and remind them of health tips.

Table 13
The sensitivity analyses on case study parameters.

No. of samples	$\#c_{w'}\#c_{w''m}\#c_{w_{whm}}\#c_{t_{gum}}$	First objective function	Second objective function	Third objective function
S1	#100#150#200	5432	3532	4193
S2	#150#200#250	5432	3789	4571
S3	#200#250#300	5432	4219	4853
S4	#250#300#350	5432	4567	5212
S5	#300#350#400	5432	4981	5316
No. of samples	w_e	First objective function	Second objective function	Third objective function
S1	0.3	5432	3532	4193
S2	0.4	5678	3532	4065
S3	0.65	5941	3532	3864
S4	0.75	6743	3532	3765
S5	0.95	6931	3532	3217
No. of samples	d_{hmt}	First objective function	Second objective function	Third objective function
S1	3346	59760	39740	5750
S2	3896	64710	48750	6150
S3	4234	69250	61280	7450
S4	4976	72360	77290	8270
S5	5839	76460	86910	9390
No. of samples	$\#c_{p_{gm}}\#vol_{mu}$	First objective function	Second objective function	Third objective function
S1	#500#500	5432	5985	4193
S2	#1000#1000	5578	5253	4065
S3	#2000#2000	5599	4974	3864
S4	#3000#3000	5656	3681	3765
S5	#4000#4000	5731	3247	3217
No. of samples	$\#em_{wt}\#cr_m$	First objective function	Second objective function	Third objective function
S1	#100#0.2	5439	3579	4216
S2	#120#0.4	5439	3897	4216
S3	#140#0.6	5439	4168	4216
S4	#160#0.8	5439	5187	4219
S5	#200#1	5439	6675	4223
No. of samples	vol'_{ml}	First objective function	Second objective function	Third objective function
S1	0.5	5467	3678	3375
S2	1	5569	4126	4198
S3	1.5	5599	4971	4935
S4	2	5670	5971	5670
S5	2.5	5708	7109	6199

Table 14
Simulation parameters and variables.

Name	Initial value	Units	Reference
Contacts rate	60	Contacts/person	Briscese et al. (2020)
Susceptible	718000	People	Pakravan-Charvadeh et al. (2020)
Death rate	4	%	World Health Organization (2020)
Disease duration	14	Days	Lauer et al. (2020)
Fraction diagnosed	40	%	World Health Organization (2020)
Rate of recovery	90	%	Chen et al. (2020a,b)

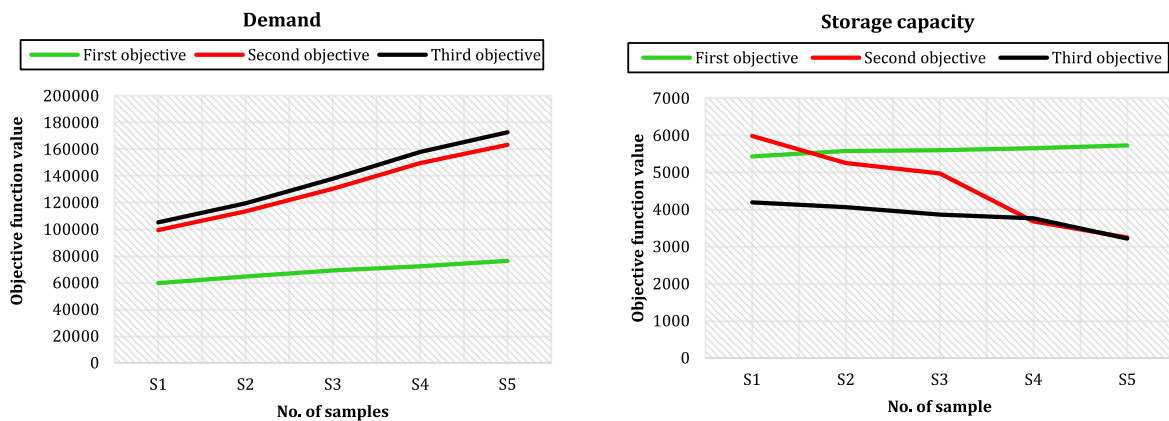


Fig. 16. The results of the sensitivity analysis of demand and storage capacity of medicine parameters.

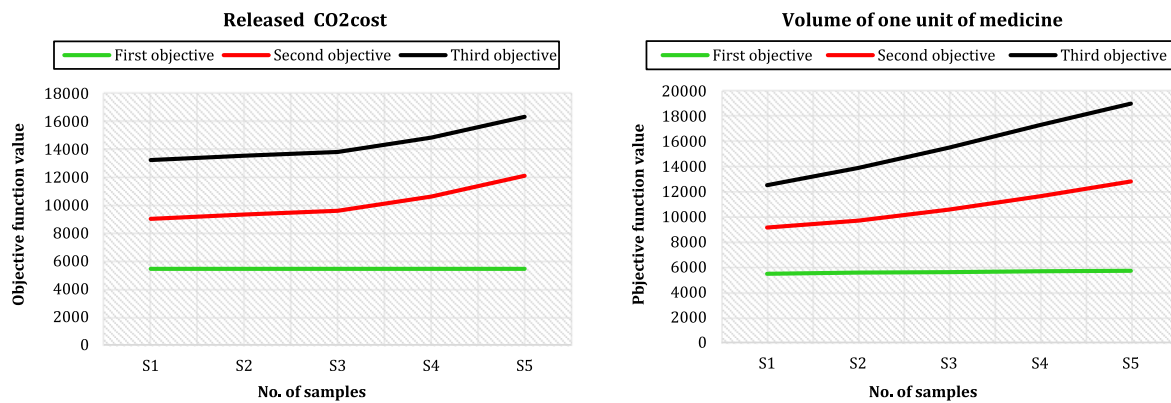


Fig. 17. The results of the sensitivity analysis of released CO₂ cost and the volume of one unit of medicine parameters.

Table 15
What-If analysis.

Scenarios	% change			
% contacts rate	-30%	-10%	+10%	+30%
% Demand changes	-63%	-28%	+25%	+57%
% susceptible	-30%	-10%	+10%	+30%
% Demand changes	-39%	-16%	+23%	+42%
% Death rate	-30%	-10%	+10%	+30%
% Demand changes	-32%	-14%	+16%	+35%
% Disease duration	-30%	-10%	+10%	+30%
% Demand changes	-45%	-18%	+21%	+42%
% Fraction diagnosed	-30%	-10%	+10%	+30%
% Demand changes	-30%	-10%	+10%	+30%
% Rate of recovery	-30%	-10%	+10%	+30%
% Demand changes	+56%	+27%	-24%	-52%

8.9. Discussion and managerial insights

According to the literature, most papers about the COVID-19 pandemic suffer from a lack of mathematical modeling. Therefore, in this paper, we developed a new multi-period multi-products multi-echelon sustainable medical supply chain network related to the COVID-19 pandemic outbreak for a new production–distribution–allocation–location–inventory holding problem. So, the considered network is divided into four echelons including laboratories, permanent centers, distribution centers, and hospitals. In the proposed model, three pillars of sustainability have been considered containing economic aspects, environmental effects, and social impacts during the COVID-19 pandemic. In terms of the economic aspects, the available costs in SMSCN including the cost of the establishing DCs, inventory holding costs, transportation costs, production costs in the medicine production laboratory, shortage costs, and surplus costs. Additionally, these economic aspects decrease the cost of released carbon dioxide from the establishment of DC and the transportation of medicine, which is considered for the first time in this paper while did not consider in other examined papers in the literature. From the view of the social effects, social factors, job creation, and economic regional development during COVID-19 conditions have been considered, simultaneously, while in the examined studies in the literature have been provided just job creation aspect or did not use. In this regard, the surveyed papers in the literature did not consider the simulation approach for the COVID-19 situation, while we have been developed a new integrated simulation-based optimization technique for the SMSCN problem. Likewise, there is the uncertainty of medicine demand during the COVID-19 pandemic that the simulation method is used to compute the demand distribution function of the needed medicines for the first time in this paper. To solve this problem, three heuristic methods based on meta-heuristic algorithms for the first time are extended but were not employed in the examined studies. Hence, original meta-heuristic algorithms are powerful algorithms in local search but at times it may trap some local

optima so that it cannot perform global search well. The reason for developing hybrid algorithms is the hybrid meta-heuristic algorithms possess a better capability to escape from local optimums with faster convergence than the original meta-heuristic algorithms. These new hybrid algorithms can speed up the global convergence rate without losing the strong robustness of the original algorithms. The main goal is to speed up the algorithm convergence and therefore to provide a more efficient tool for a wider range of practical applications while preserving the attractive characteristics of the original meta-heuristic algorithms. To validate the presented hybrid algorithms, six assessment metrics involving IGD, SNS, MS, MID, NPS, HV have been utilized, which the results of the suggested metrics show that the HFSA-VNS algorithm had high significant performance and efficiency. In addition, in order to closer to the real-world, a real case study about the COVID-19 pandemic situation in Tehran/Iran has been examined.

It is assumed that all of these environmental outcomes are short-term. Therefore, it is high time to make an appropriate strategy for sustainable environmental management, and also the long-term benefit. The outbreak of the COVID-19 pandemic makes us united to win against the virus and has elicited a global response. Likewise, to protect the home of human beings, the united effort of the countries and this globe should be imperative (Rume and Islam, 2020). Moreover, some possible strategies for global environmental sustainability are shown in Fig. 18.

Therefore, the pandemic is affecting the global economy and human life directly or indirectly, which is ultimately affecting the environment and climate. It reminds us how we have neglected enforced human-induced climate change and the environmental components. Therefore, the global answer of COVID-19 also teaches us to work together to struggle with the threat to mankind. Although the effects of COVID-19 on the environment are united, short-term, and proposed time-oriented efforts can strengthen environmental sustainability and save the earth from the effects of global climate change.

Industrialization for economic growth is important and significant; however, it is time to think about sustainability. In terms of the sustainable industrialization, industries should be built in some special areas, keeping in mind that waste from one industry (i.e., pharmaceutical industry) can be utilized as raw materials of the other. After a certain period, industrial areas should have been shut down in a circular way to decrease emissions without hampering the national economy. Therefore, industries especially pharmaceutical companies and others where a huge number of people work, proper distance, and hygienic environment should maintain to decrease the spread of any infectious communicable disease. In addition, it is necessary to shift to less energy-intensive industries, and strong energy efficient policies, utilize cleaner fuels and technologies.

From the view of utilizing public transport and green concepts, to decrease emissions and CO₂, it is essential to encourage people to utilize public transport, rather than private vehicles. Furthermore, people

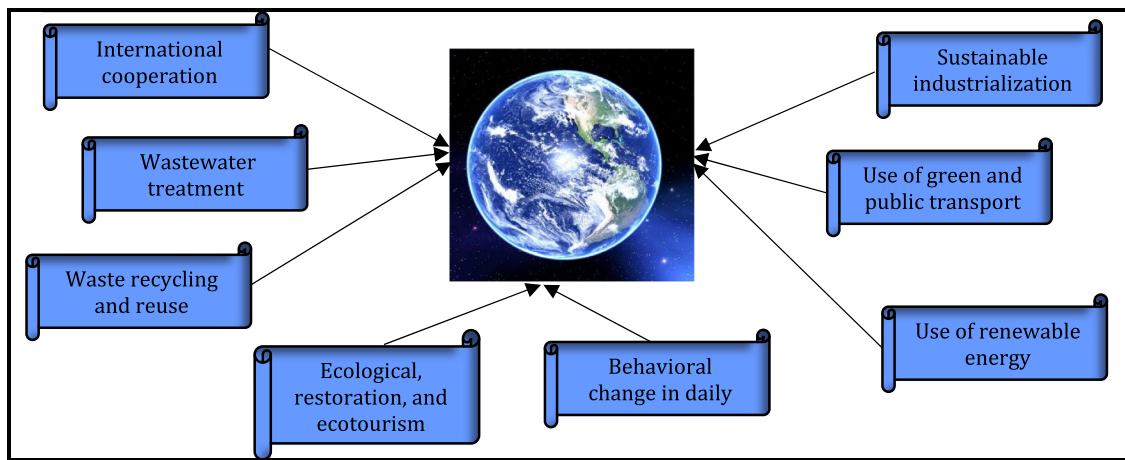


Fig. 18. The presented strategies of sustainable environmental management.

should encourage to utilize bicycles a short distance, and a public bike-sharing system should be existing for mass utilization, which is not only environmentally useful but also beneficial for health. The pros and cons of the proposed meta-heuristic algorithms and simulation approach are explained as follows:

Advantages

- The proposed meta-heuristic algorithms are flexible and adaptable to the types of objective functions and solution spaces.
- The proposed meta-heuristic algorithms use only the values of the objective functions to solve the models and do not require more information such as the derivative of the functions, which causes the proposed algorithms were easy and user-friendly.
- According to the high speed of the search process, the proposed algorithms have a high speed of convergence.
- Meta-heuristic algorithms have the ability to handle random types of objectives and constraints and also can be utilized to handle problems whose constraints and objective functions are nonlinear or discontinuous.
- The used Enterprise Dynamic software in this paper by using 4D Script programming language can solve all types of simulation problems and has a high convergence speed.
- The simulation model implementation type is a separate run. For this purpose, the model is run multiple times and the average results are presented that causes minimize the percentage of simulation error as much as possible.
- The open-source structure of the simulation software allows atoms to be customized, which makes the simulation closer to the real world.

Disadvantages

- Meta-heuristic algorithms calculate local optimal solutions and are not able to calculate the global optimum.
- The local solutions of the presented hybrid/heuristic approaches in this paper depend on the coder's skill in finding the initial solution.
- According to the numerous implementations in the simulation model, computers with high RAM and CPU are required while this approach is very time consuming and costly.

9. Conclusion and future works

In this research, the first novelty, a new integrated simulation-optimization model of a multi-objective, multi-level, multi-product,

and multi-period SMSN problem is developed. The main aims including to maximize social factors, job creation, and economic regional development, to minimize the costs of establishing distribution centers, inventory holding, transportation costs, production cost in the medicine production laboratory, shortage and surplus costs with decreases the cost of released carbon dioxide from the establishment of DC and the transportation of medicine, and to minimize the maximum unmet demand of medicines are illustrated. The suggested production–distribution–inventory–allocation–location network is recognized of four levels containing hospitals, permanent centers, the medicine production laboratory, and distribution centers. The second important novelty, three meta-heuristic algorithms (i.e., HACO-VNS, HFSA-VNS, and HFA-VNS, which are Ant Colony Optimization (ACO), Fish Swarm Algorithm (FSA), and Firefly Algorithm (FA), each hybridized with variable neighborhood search (VNS) are proposed to tackle the addressed problem. The parameters of the algorithms are estimated by response surface method according to the six various assessment metrics are computed and analyzed. are computed and analyzed. Then, it was cleared that the HFSA-VNS dominates the outcomes of HACO-VNS and HFA-VNS based on the attained outcomes. In all assessment metrics, HFSA-VNS does better than other proposed algorithms. Another contribution of this study is to investigate the system dynamic structure of the COVID-19 outbreak and to estimate the number of required medicines, using the simulation approach. A case study in Iran represents the validity and application of the presented model. In this paper, the distribution function of required medicine for COVID-19 patients follows the Normal distribution function with an average of 3325.14 and a variance of 136.2 according to the simulation results.

As future works, developing new meta-heuristic algorithms and comparing them with these hybrid algorithms is attractive. Scholars can add an ordering policy during the COVID-19 pandemic to the SMSN model. Additionally, we suggested resiliency concepts, which can be added to the proposed model in future works. As such, our paper has the potential for adoption by other fields containing medical industrial and healthcare networks. For example, blockchain technology coupled with suitable approaches can significantly improve the implementation of health care networks, due to its ability to manage patient data and prescriptions. Therefore, such platforms can direct patients to take the correct medicine at the right dosages. The incorporation of blockchain technology into applications can thus improve user safety. The potential applications are endless. We hope that this paper offers inspiration and motivation for continued advancements in this field. Researchers can also utilize uncertainty programming such as robust, fuzzy, possibilistic, and possible techniques.

CRedit authorship contribution statement

Fariba Goodarzian: Conceptualization, Methodology, Software, Data curation, Writing - original draft, Formal analysis, Validation. **Ata Allah Taleizadeh:** Supervision. **Peiman Ghasemi:** Supervision, Data curation, Writing - review & editing. **Ajith Abraham:** Supervision, Editing the paper.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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